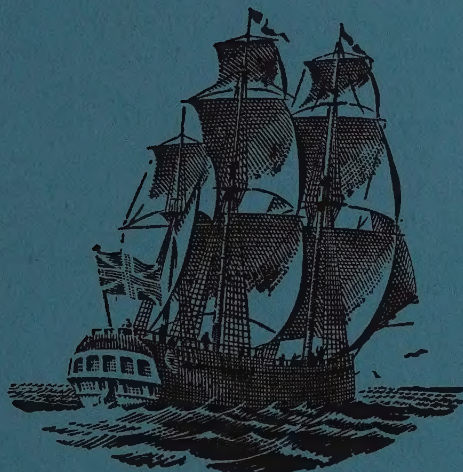
ENDEAVOUR



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ENDEAVOUR

The British quarterly scientific journal ENDEAVOUR was first published, by Imperial Chemical Industries Limited, in January 1942. Its purpose is to provide scientists, especially those overseas, with news of the progress of the sciences. While emphasis is laid upon British work, narrow insularity is avoided by publishing numerous articles from overseas contributors and by impartial reference to the world's scientific literature. To make the journal truly international in character it is published in five separate editions—English, French, German, Italian, and Spanish.

No charge is made for ENDEAVOUR. It is distributed to senior scientists, scientific institutions, and libraries throughout the world, the guiding principle being that of helping scientists overseas to maintain those contacts which their British colleagues have always so much valued. Within these limits the Editors are at all times glad to consider the addition of new names to the mailing list.

The drawing on the cover is of the bark Endeavour, *which, commanded by Captain James Cook and carrying a number of scientific workers, was sent out by the British Admiralty in* 1768 *to chart the South Pacific Ocean and observe the transit of Venus*

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

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The Royal Society of Arts

This year marks the bicentenary of the Royal Society of Arts, the history of which is related in a book written by Derek Hudson and Kenneth W. Luckhurst and recently published.[1] The Society was born at a time of great industrial and commercial activity, when local crafts were beginning to give ground before the advance of mechanized factories, and when 'almost every Master-Manufacturer hath a new Invention of his own, and is daily improving on those of others'. These conditions led to the founding of various technical societies for the study of trade, industry, and the industrial arts, and the Royal Society of Arts was one of the first of such associations to be established in Great Britain.

The idea of the Society was conceived by William Shipley (1714–1803), brother of the then Bishop of St Asaph and a friend of Benjamin Franklin; he was an obscure drawing-master at Northampton. In the beginning, Shipley's plan was that industry should be stimulated by prizes drawn from a fund contributed by public-spirited people, but, as so often happens, the first step towards the realization of the project was the most difficult. Full of enthusiasm, however, Shipley obtained an introduction to Stephen Hales, the distinguished author of 'Vegetable Statics', and was fortunate enough to meet with encouragement. Hales mentioned the matter to influential friends, and on 22 March, 1754, at a meeting at a coffee-house in Covent Garden, it was decided to form a society 'for the Encouragement of Arts, Manufactures and Commerce'. This title, with the addition of 'Royal' in 1908, has been the official designation of the Society ever since, though it has always been more familiarly known by the abbreviated version, 'Society of Arts'.

The Society clearly supplied a great want, for it grew with astonishing rapidity, and by 1762 had a membership of over 2500; among the earliest members were such well known figures as Thomas Chippendale, Robert Clive, Edward Gibbon, William Hogarth, Samuel Johnson, Joshua Reynolds, Samuel Richardson, and Horace Walpole.

One of the reasons for the Society's speedy rise to eminence was that, in the eighteenth century, there were no departments of state or other institutions to deal with such affairs as agriculture, forestry, trade, industrial art and science, and many other public matters that are today the concern of various specialist bodies; moreover, public-spirited men welcomed the opportunity offered by the new society to serve their country in ways not previously envisaged.

For nearly a hundred years the Society followed Shipley's plan of 'encouragement' by offering premiums for specified purposes, and the annual prize-giving became one of the major social events of the season during the earlier part of the nineteenth century; in 1848 no less a person than the Prince Consort made the presentations. Among the Society's efforts, none was promoted more energetically than that devoted to the improvement of agriculture, where it was fortunate enough to secure the services of Arthur Young, the famous agriculturist, as chairman of its appropriate committee. It may be said with truth that the British agricultural revolution of the eighteenth century was in the main effected through the influence of the Society, which offered prizes for such objects as the improvement of agricultural machinery, the production and use of manures, better methods of cultivation, and many other aspects of what we now call agricultural science.

A related subject in which the Society took much interest was afforestation. At the time when the Society was founded there was a serious shortage of timber for fuel and shipbuilding, and the matter was one of national concern. By the offer of medals, themselves of little intrinsic value but carrying much honour, the Society induced wealthy landowners to embark upon ambitious programmes of afforestation. From 1758 to 1821 the Society awarded 127 gold medals and 40 silver medals for these activities, and the number of trees planted during this period was at least fifty million. Many of the woods in Great Britain today owe their existence to the Society of Arts.

Among early members of the Society were several distinguished chemists, and the chemistry committee was one of the most important. Then, as now, sulphuric acid and alkalis were in great demand for industrial purposes, and though Ward and Roebuck had improved methods of manufacturing the acid, greater supplies of alkali were a pressing need. The Society attempted to meet this need by encouraging the production of alkali from home vegetable sources, and by importation from the American colonies. Better success attended its efforts for the refinement of whale oil and

[1] 'The Royal Society of Arts, 1754–1954.' *John Murray, London.* 1954. 30*s. net.*

the manufacture of verdigris, and its far-sightedness is attested by its award, in 1808, of a silver medal to Samuel Clegg, inventor of the modern type of gas-holder and of the gas-meter, for a paper on schemes of gas-lighting in factories and public buildings. At about the same time, the Society awarded a silver medal to a Birmingham man for his coal-tar distillation process. It is worthy of note that early meetings of The Chemical Society were held in the premises of the Society of Arts.

Far-sightedness was also shown by the Society in its encouragement of art in the narrower sense of the word. Even at its first meeting the opinion was expressed that the art of drawing 'is absolutely necessary' in trade and industry, and at the next meeting the decision was taken to include prizes for drawings by children in the first list of premiums to be offered. Among the youthful prizewinners, of average age 13, were Landseer, Millais, Lawrence, and Eastlake, the last three of whom later became presidents of the Royal Academy. In 1760 the Society organized the first public exhibition of contemporary art to be held in Britain. The exhibition was a striking success, and the stimulus it provided led to the foundation of the Royal Academy only eight years afterwards.

Its experience in 1760 convinced the Society of the value of exhibitions, which have formed a principal feature of its activities throughout its life. In 1761 it staged the first British industrial exhibition, a display of agricultural machinery, but its most resounding success was the Great Exhibition of 1851. This seems to have been the personal inspiration of the Prince Consort, who was then president of the Society and who felt that the exhibition should be on international rather than national lines. The final management of the Great Exhibition was taken over by a Royal Commission, but the chief credit for it must certainly be given to the Society.

The Society soon extended its interests beyond the limits of Britain to British possessions overseas, and awards were offered to help the colonies either by encouraging the introduction there of new plants and industries, or by promoting the export of colonial produce to Britain. The famous expedition of the *Bounty* originated from the Society's offer of a prize for the successful transplanting of the bread-fruit tree to the West Indies. The commander of the *Bounty*, Captain Bligh, was not to succeed on this occasion, but on a second expedition, in the *Providence*, he successfully transplanted not only bread-fruit trees but very many other valuable plants to the West Indies; he was awarded the Society's gold medal. Some thirty years later, in 1820, the Society offered two further gold medals, one for the largest quantity of fine wool imported from New South Wales and a second for the finest sample of wool from that colony; both were awarded in 1822 to John Macarthur, founder of the Australian wool trade which now plays so great a part in Commonwealth and international commerce. The Society also encouraged the early wine industries of South Africa and Australia, and tea cultivation in India.

Such a sweep of achievements, in so many and such diverse fields, might seem ample to satisfy the ambitions of several societies, not merely those of one; but the Society of Arts went, and goes, from strength to strength. Whatever the task, the Society has always been willing to attempt it, if its accomplishment seemed to be likely to benefit the arts, the sciences, trade and industry, education, or public health. For example, it was responsible for the abolition in Britain of the practice of sweeping chimneys by sending small boys up them, and for the introduction of the chimney-sweep's extending flue-brush; it also, in 1851, pioneered and established the system of public lavatories—one of the civic amenities that perhaps are hardly thought of as having had to be deliberately inaugurated. The Society further made possible a microscope that sold for half a guinea, and a box of paints for a shilling: eleven million of these boxes were sold between 1851 and 1870.

There are, indeed, few cultural or industrial fields in which the beneficent and beneficial influence of the Society of Arts has not been felt. The founding of the Royal College of Music and that of the Royal Photographic Society stand to its credit, and such miscellaneous affairs as the printing of bank-notes, life-saving at sea, cartography, shipbuilding, the construction of scientific instruments, the design of textile machinery, postal reform, and the supply of fresh fish to London all figure in its list of agenda. The lectures delivered under its aegis by leading authorities on their subjects cover all branches of arts, manufactures, and commerce, and are invariably well attended.

The bicentenary volume by Hudson and Luckhurst gives an absorbing account of the two hundred years of the Society's life and manifold activities, enriched by the inclusion of many illustrations. Here we have been able to give only a sketch of what is surely one of the most remarkable societies in the world. Under its present president, H.R.H. the Duke of Edinburgh, it enters its third century with undiminished vigour and confident purpose.

The viscosity of liquids

E. N. DA C. ANDRADE

The viscous properties of liquids offer peculiar difficulties to the theoretical physicist who wishes to deduce them from the conventional laws of molecular interaction. Examination of the experimental results has, however, revealed a number of general regularities, especially where the variation of viscosity with temperature is concerned, and, in the case of the less complex liquids, some approach has been made to an explanation along simple lines.

INTRODUCTION

The liquid state, as contrasted with the gaseous state, and with the solid state in certain of its aspects, offers peculiar difficulties. The measured properties of gases, especially under conditions not too near the critical point, exhibit many simple and striking regularities which, in the main, have found a satisfactory representation in terms of the kinetic theory. Here the fact that the molecules are for the greater part of the time travelling at uniform speeds in a region where the intermolecular forces are negligible introduces great simplifications. Only encounters involving two, not more, molecules need be considered; since the relative orientation of two molecules involved in collision is random, the shape of the molecules is of little influence; when mechanical properties are in question it is generally possible to neglect the vibrations and rotations of the molecules; and when specific heats are concerned the part that they play can be taken into account. All these simplifying factors are absent when we come to consider liquids.

With solids—that is, crystalline solids—matters are simplified by the high degree of order in space of the atoms and molecules. Properties such as specific heat are independent of small faults or irregularities in the crystal structure. The mechanical behaviour, on the other hand, is an example of a class of properties known as structure-sensitive, for which local lattice irregularities have a supreme significance, involving the complication that the properties depend markedly upon the previous history of the specimen. Here liquids have an advantage, for with homogeneous liquids the constants concerned in flow are uniquely determined by the state—pressure and temperature—of the substance. Except in the relatively trivial cases of supercooling and superheating, thermodynamically unstable states do not occur. A study of the viscosity of liquids, then, seems a possible source of significant information concerning the nature of the liquid state and, as will be seen, does reveal certain striking general regularities.

HISTORICAL

The history of viscosity as a branch of physics starts with Newton, when, in the Second Book of the *Principia*, he treats of fluids maintained in circular motion either by an infinitely long rotating cylinder or by a rotating sphere. His object was to investigate the properties of the Cartesian solar vortex of subtle fluid, which, by its motion, carried the planets round. He arrived at the conclusion '*Hinc liquet Planetas à Vorticibus corporeis non deferri*'—'Hence it is manifest that the planets are not carried round by material vortices' [1]. What is of interest here is that for the purpose of the calculation it is necessary to assume a law according to which the motion of one layer of liquid is transferred to a contiguous layer, and Newton stated as his hypothesis '*Resistentiam, quae oritur ex defectu lubricitatis partium Fluidi, caeteris paribus, proportionalem esse velocitati, qua partes Fluidi separantur ab invicem*'—'The resistance arising from the want of slipperiness in the parts of the fluid is, other things being equal, proportional to the velocity with which the parts of the liquid are separated one from another' [2]. The fluid in Newton's treatment was divided into 'innumerable' sheets of equal thickness, so that this assumption meant that the resistance to shearing motion was proportional to the velocity gradient. Liquids for which this is true are accordingly said to possess Newtonian viscosity.

Newton did not apply to real liquids the considerations that followed from his assumption, and for more than a century after the publication of the *Principia* those who dealt with the motion of fluids left out all considerations of liquid friction. At the very end of the eighteenth century and the beginning of the nineteenth, French investigators, Coulomb and Girard in particular,

carried out well-designed experiments on the resistance to motion offered by liquids, but without any attempt to analyse the movement. Navier, the founder of the modern mathematical theory of elasticity, in 1823, 136 years after Newton, restated Newton's law of fluid resistance without, apparently, any knowledge of what Newton had done, and defined, without giving it a name, a constant ε which is our coefficient of viscosity. It was, in particular, Stokes [3] who in 1845 created the modern theory of the motion of viscous liquids: for instance, starting with Newton's assumption he worked out in essence the flow through a cylindrical tube, the example most familiar to students of today who use capillary viscometers. Just about this time Poiseuille [4] published his classic work on the flow of liquids through tubes. He was a doctor of medicine interested in the flow of blood through capillaries, a fact which had the fortunate consequence that, so as to compare with the anatomical vessels, he used much finer tubes than his predecessors, the diameters ranging from 0·14 to 0·03 mm. He worked with distilled water and obtained experimentally the well known formula for the volume V discharged in unit time:

$$V = C\frac{pr^4}{l},$$

where C is a constant, p is the pressure difference at the two ends of the tube, r is the radius, and l is the length. He also measured systematically the variation of the volume V with the temperature, from 0° to 45° C. Poiseuille's work was of great accuracy, and marks an important stage in the development of the subject. It is, perhaps, strange that the study of viscosity should start theoretically with an interest in Descartes' hypothetical celestial medium and experimentally with an interest in the flow of blood, the macrocosm and the microcosm thus coming together in true alchemical fashion. '*Blut ist ein ganz besondrer Saft.*'

The first use of the term coefficient of viscosity that I can find is by Clerk Maxwell [5], when, in connection with his investigations into the mechanical behaviour of gases, he defines it in 1866: in 1860, discussing the same subject, he speaks of internal friction (which recalls the German *innere Reibung*) and coefficient of friction. In these slight historical notes many noteworthy names have been omitted, but something must be said of Thorpe and Rodger [6], who, in the 1890's, made a determined attack on the problem of the relationship between the viscosity of liquids and their chemical nature. Their work occupies about 350 pages in the 'Philosophical Transactions' of the Royal Society and comprises very careful determinations of the viscosities, at various temperatures, of 88 liquids of definite chemical composition, mostly organic compounds. In many cases their values are still the best available. The great weakness of the measurements is that, while the upper limit of the temperature range is somewhere near the boiling-point of each particular liquid, the lower limit is in all cases 0° C. This means that for liquids with low boiling-points the temperature range is very small, but, worse than this, as the freezing-points of the majority of the liquids are 50° C or more—in many cases 100° C or more—below 0° C, it is very seldom that reliable values of the viscosity are available in the neighbourhood of the freezing-point which, as will be argued, is a very interesting region.

Thorpe and Rodger, in their attempt to relate viscosity and chemical nature, wished to make a comparison of viscosities at what they called comparable temperatures and were faced with the question as to what were such temperatures. Influenced, no doubt, by the measurements, they selected the boiling-point, which seems unfortunate, since it is influenced so much by pressures of an order that leaves the viscosity unchanged. Having little success with viscosities at boiling-point they tried other methods of comparison, in particular of viscosities at 0·6θ, where θ is the critical temperature of the liquid, and also of viscosities at points where the slope of the viscosity-temperature curve, $d\eta/dt$, was the same; in general, however, it cannot be claimed that they found any noteworthy regularities in their heroic onslaught on the problem.

Later, Dunstan and Thole [7], taking 20° C as a standard temperature for all liquids, found certain empirical rules for predicting the viscosity at this temperature within a homologous series, results of interest which, however, did not lead to any generalities on liquid viscosity.

VARIATION OF VISCOSITY WITH TEMPERATURE

The most striking feature of liquid viscosity is the very marked way in which it decreases with rise of temperature, whereas the viscosity of gases increases with temperature. A generality seems to be that, roughly speaking, the more complicated the liquid the greater the influence of temperature. Thus with certain glasses, in the temperature range where they behave as normal, but very viscous, liquids, a rise of 100° C diminishes the

viscosity to 1000th or even much less; with a strong sucrose solution the viscosity falls to 1/70 when the temperature rises from 0° to 100° C; with a certain amyl alcohol to 1/18; with one of the octanes to 1/3; with bromine to 2/5; and with mercury to 5/7, for the same temperature interval. The liquid metals and monomolecular liquids in general show a comparatively small variation of viscosity with temperature: with liquid gallium a change of temperature of over 1000° C, from 80° to 1100° C, reduces the viscosity to 1/3.

When we turn to the question of a precise representation of the variation of viscosity with temperature we are met with a variety of formulae. One class of formula regards the change with temperature as entirely due to the change of volume. Typical of this class is Batschinski's formula [8]:

$$\eta = \frac{c}{v - w},$$

where c and w are constants. Here v is the specific volume and w a limiting volume at which η becomes infinite. The expression $v - w$ is called the free volume: values for it can be derived from other formulae, but the results of different methods do not agree very well. The essential objection to formulae of this type is that, as is clear from Bridgman's work [9] on the viscosity of liquids at high pressure, the viscosity is not a function of the volume alone. Thus figure 1 shows the viscosity of isoamyl alcohol against volume at two different temperatures; it will be seen that there are two well separated curves. Nevertheless, volume-dependent formulae are still occasionally advocated [10].

Thorpe and Rodger used Slotte's formula [8] $\eta = C/(1 + bt)^n$, where t is the temperature in °C and there are three constants, but did not find it very satisfactory and adopted another three-constant formula. Duff [11] in 1897 quoted seven formulae which had been proposed and himself added an eighth, with four constants. After him Brillouin produced a formula with five constants, somewhat too many if we are seeking for simple regularities.

In 1930 Andrade [12] put forward the simple exponential formula

$$\eta = Be^{b/T} \ldots\ldots\ldots\ldots\ldots (1)$$

to represent the variation of viscosity at constant pressure with temperature. This he later [15] modified to

$$\eta v^{\frac{1}{3}} = Ce^{c/vT} \ldots\ldots\ldots\ldots (2)$$

to take account of the change in volume which accompanies change in temperature. It subsequently appeared that the simple exponential formula (1) had been put forward by de Guzman [13] in 1913: he took Kirchhoff's formula for the vapour pressure, $\log p = A - B/T - C \log T$, omitted the last term, and substituted φ for p. There does not seem to be any reason why the vapour pressure formula should apply to liquid viscosity and de Guzman's work never attracted attention, not being mentioned in any of the textbooks dealing especially with viscosity. The early history of the formula is discussed in a series of letters in 'Nature' [14].

Andrade [15] made a systematic comparison of formula (2) with the experimental results of Thorpe and Rodger, and others. Where the range of measurement, expressed as the ratio of the highest measured η to the lowest, was 2 or less, the agreement was, in general, everywhere within 0·3 per cent; for ranges up to 3, within 1 per cent; and even in more extended ranges the deviation seldom exceeded 2 per cent. In the case of normal propyl alcohol from — 60° to 96° C, where the viscosity goes from 0·319 to 0·0047 poise, a range of 67, the largest error was 2·2 per cent. In general, it must be remembered that viscosity is not a property that has been measured to a high degree of accuracy. For the liquids in question the measurements have practically all been made with some form of capillary viscometer, where the fourth power of the radius is involved, and a somewhat uncertain end-correction, depending upon the

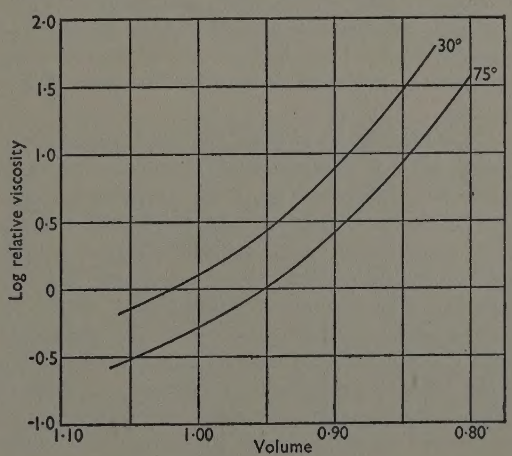

FIGURE 1 – *The variation of viscosity of isoamyl alcohol with volume at 30° and 75° C, derived from Bridgman's high-pressure results. The graph shows log η/η_0 against v, where η_0 is the viscosity at 30° and atmospheric pressure.* (P. W. BRIDGMAN, '*The Physics of High Pressure.*' *G. Bell and Sons Limited, London.*)

volume passing through per second, is also necessary. It is not only in absolute measurements that these factors are concerned, for both the radius and the end-correction change with temperature, especially the latter. Viscosities given to five significant figures are expressions of a genial optimism.

The general fit of the two-constant formula can, then, be claimed to be good for a variety of liquids, including liquid metals, alkyl and alkenyl halides, thioethers, primary and secondary alcohols, esters, aromatic hydrocarbons, and fatty acids. Exceptional liquids are water—of course—and tertiary alcohols, which are anomalous in other respects. It looks as if water behaves normally above 70° [12], but the range of measurements at present available is not large enough for a definite decision.

The formula $\eta = Be^{b/T}$ is widely used to represent the variation of viscosity, since it is very simple to apply. Formula (2) gives, in general, a slightly better fit when the range of viscosity is large, but the best evidence for its validity is offered by the viscosity of the series of liquid alkali metals, considered later.

GENERAL THEORETICAL CONSIDERATIONS

The exponential formula, being valid for such a wide range of liquids, in many cases with molecules of considerable complexity, seems unlikely to depend upon any particular assumption as to details of intermolecular forces. The point of view on which it was based when originally put forward is not, perhaps, unexceptionable, but it led to formulae which have had success in representing experiment, and this is one justification of hypothesis.

The molecules were regarded as vibrating, as a whole, with a fundamental frequency ν, each about an equilibrium position that moved only slowly. With a monomolecular solid, such as lead, there are various ways of estimating ν, which agree in giving a value about $2{\cdot}0 \times 10^{12}$ for this element. The change of volume of a metal on melting being comparatively small, the molecular forces cannot be very different in the two states at the melting-point, at any rate for elements of cubic, or nearly cubic, crystal structure, and so the frequencies must be much the same. From the coefficient of self-diffusion, measured by the help of radioactive isotopes, it appears that for an atom of liquid lead to diffuse through a distance σ, where σ^3 is the average volume of liquid per atom, the time required is about 80 periods of vibration, which offers justification for the assumption of a quasi-stationary centre of vibration. It was assumed, without any detailed dynamical justification, that, at the melting-point, momentum was communicated from layer to layer of the sheared liquid at every extreme libration of the oscillation. From such an assumption it follows at once that η_M, the viscosity at the melting-point temperature is:

$$\eta_M = C\frac{\nu m}{\sigma},$$

where m is the mass of the molecule and C is a constant which must be about 1. Even with gases the constant in the viscosity formula cannot be precisely calculated except for the simplest molecules. The value 4/3 was, by a rough argument, taken for C.

There are two general ways of finding ν for monomolecular substances, such as liquid metals and noble gases, which are particularly suitable for numerical check on a simple theory. It can be expressed as $\nu = k\theta/h$, where θ is Debye's characteristic temperature, or, by a formula due to Lindemann (Lord Cherwell), as:

$$\nu = K\sqrt{\frac{T_M}{AV^{\frac{2}{3}}}},$$

where T_M is the melting-point in degrees absolute, A the atomic weight, and V the atomic volume, K having the value $3{\cdot}1 \times 10^{12}$. Accordingly the viscosity of a monomolecular liquid at the melting-point is given by

$$\eta_M = \frac{4}{3}\left(\frac{A^2\rho_M}{N^2}\right)^{\frac{1}{3}}\frac{k}{h}\theta = 3{\cdot}90 \times 10^{-6}\,\theta\rho_M^{\frac{1}{3}}A^{\frac{2}{3}} \quad \ldots\ldots (3)$$

or

$$\eta_M = 5{\cdot}7 \times 10^{-4}\,(AT_M)^{\frac{1}{2}}\,V^{-\frac{2}{3}} \quad \ldots\ldots (4)$$

The constant is in neither case arbitrary: $3{\cdot}90 \times 10^{-6}$ is the value of $\frac{4}{3}k/N^{\frac{2}{3}}h$, and $5{\cdot}7 \times 10^{-4}$ is the value of $\frac{4}{3}KN^{-\frac{2}{3}}$.

The values given by these formulae are in good agreement with the measured viscosity of monomolecular liquids at the melting-point. For instance, according to (3), the value of

$$\frac{\eta_M}{\theta\rho_M^{\frac{1}{3}}A^{\frac{2}{3}}}$$

should be $3{\cdot}90 \times 10^{-6}$ for all metals. For seven metals, Li, Na, K, Cu, Ag, Au, Pb, for which values of θ are available, the values prove to be 4·05, 4·35, 3·95, 4·05, 3·78, 3·68, 4·11, all $\times\ 10^{-6}$, although the extreme viscosities are as 1 to 10 and

the extreme densities as 1 to 34. For liquid helium I, the 'normal' form, the viscosity of which is about a thousandth of that of liquid gold, the available value of θ gives $\eta_M = 9{\cdot}5 \times 10^{-5}$ poise as against $7{\cdot}3 \times 10^{-5}$ found experimentally by Tjerkstra on the melting curve [16].

In figure 2 are shown the viscosities of sixteen liquid metals and of liquid argon at the melting-point, plotted against $(AT_M)^{\frac{1}{2}}\, V^{-\frac{2}{3}}$. It will be seen that the points lie well on a straight line, of slope $5{\cdot}7 \times 10^{-4}$, with the exception of the three metals Sb, Bi, and Ga. That these metals depart from the law is, in a way, extremely satisfactory, for they are of anomalous, far from cubic, crystal structure and, in general, freakish. For instance, the ratio of the electrical conductivity in the solid state to that in the liquid state, at the melting-point, is round about 0·5 for these three, whereas for the normal metals it has values between 1·45 and 2·28. Theory gives values for these normal metals which are in quite good agreement with experiment, but for the abnormal three it predicts values in the neighbourhood of 5, that is, about ten times too big [17]. The coefficient of thermal expansion likewise shows a very marked anomaly for the three metals.

The satisfactory agreement in absolute magnitude of observed and calculated viscosity indicates that no theory based on the communication of

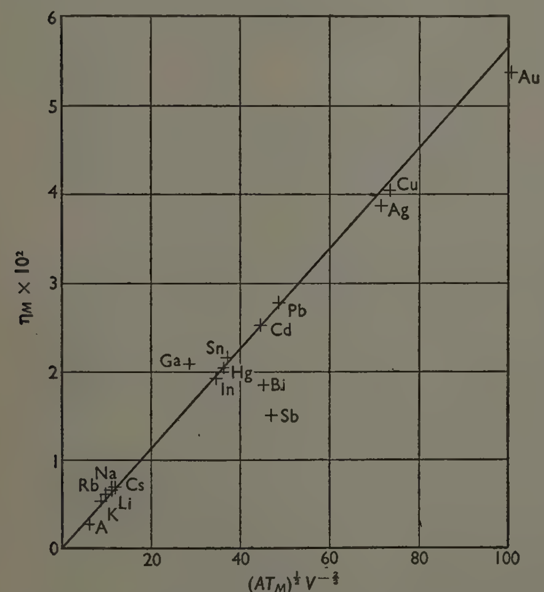

FIGURE 2 – *Viscosity of liquid metals at the melting-point against* $(AT_M)^{\frac{1}{2}}\, V^{-\frac{2}{3}}$. *The point for liquid argon is also shown.*

momentum by actual passage of the molecule from layer to layer (as in the case of gases) can be valid, for the example of liquid lead, already cited, shows that if this were the mechanism the calculated viscosity would be about a hundredth of the observed value.

To derive the temperature variation, reliance was placed on a general argument that the temperature agitation must interfere with the communication of momentum, a certain energy of orientation, or activation, being, in accordance with Boltzmann's principle, favourable for this communication. The ratio of the number of molecules possessing the required energy E at temperature T to that at T_1 must then be

$$e^{\frac{E}{k}\left(\frac{1}{T}-\frac{1}{T_1}\right)}$$

so that
$$\eta = \eta_{T_1} e^{-E/kT_1} e^{E/kT}.$$

If T_1 is the melting-point T_M, then

$$\eta = \eta_M e^{-E/kT_M} e^{E/kT}$$
$$= Be^{E/kT} = Be^{b/T}.$$

If we take into account the expansion which takes place when the liquid is heated, there are three effects to be considered: the number of molecules per unit area of the plane of shear decreases, the distance between two molecular layers increases, and the mutual potential energy decreases. The average potential energy of a molecule varies, by the Van der Waals equation, inversely as v, the specific volume. If we make our viscous 'activation' energy vary in this way we get for the formula for temperature variation:

$$\eta v^{\frac{1}{3}} = Ce^{E/vkT} = Ce^{c/vT},$$

which has been proved generally successful.

The strongest experimental argument that this gives a better representation of the mechanism than the simple exponential formula (1) is provided by the liquid alkali metals [18]. Both formulae give a good representation of the variation of viscosity with temperature for each individual metal, thus providing values of the exponential constants b and c. However, whereas c diminishes smoothly with increasing atomic weight, b shows a very irregular behaviour (figure 3). The values of the multiplying constants B and C also indicate that (4) is the preferable formula.

If we consider monomolecular liquids, and use formula (4) for η_M, we get:

$$\eta = 1{\cdot}33 e^{-C/v_M T_M} \frac{\sigma_M}{\sigma} \frac{m v_M}{\sigma_M} e^{c/vT},$$

which compares with the formula derived by Born and Green [19]:

$$\eta \sim \frac{\pi^2}{315} (42\pi)^{\frac{1}{2}} \left(\frac{\sigma_M}{\sigma}\right)^5 \frac{mv_M}{\sigma_M} e^{-\phi(v)/kT},$$

the chief difference being that σ_M/σ appears to the fifth power in this formula and the more general $\varphi(v)$, which cannot be used for numerical calculation, replaces v^{-1}.

KINETIC THEORIES OF THE LIQUID STATE

Something should here be said about certain recent theoretical developments. The strict mathematical theory of the liquid state aims at deducing the properties of liquids from a molecular mechanism, in particular from the potential $\varphi(r)$ of mutual interaction between the molecules and from their distribution. In the case of the so-called transport phenomena, viscosity and thermal conductivity, an essential consideration is the distortion of the equilibrium distribution, a distortion produced by the velocity gradient in the case of viscosity and, less seriously, by the temperature gradient in the case of thermal conductivity. The problem has been handled, in particular, by Kirkwood, by Eisenschitz, and by Born and Green [20]. Kirkwood, starting from fundamental considerations, has simplified matters by the useful and ingenious assumption that the forces on a molecule at different instants are statistically independent, provided that the time interval between the instants is not too small, but he has not established any relation between viscosity and temperature. Eisenschitz has modified the theory of Brownian motion so as to make it apply to a single molecule and is met, of course, by the difficulty as to what is the friction constant (or rather as to what are the friction constants, for he points out that there are two), a matter with which Kirkwood has also dealt. Born and Green have developed an imposing theory based on distribution functions, which is not always easy to follow, especially in the matter of the assumptions made in dealing with viscosity.

Eisenschitz, and Born and Green, arrive at an exponential function for the variation of viscosity with temperature. The work of Eisenschitz leads to the conclusion that there is no such exponential factor in the thermal conductivity, but some relatively slowly varying function, which is in accord with experiment. None of those, however, approaching the matter from fundamental considerations of the type indicated has been able to produce results that can be checked quantitatively by

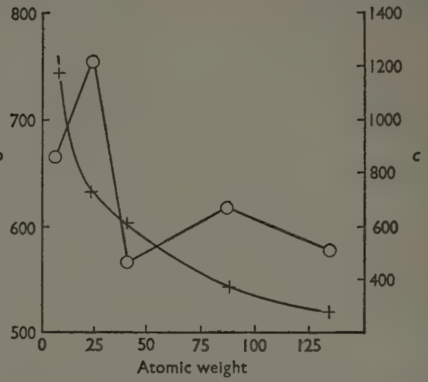

FIGURE 3 – *The constants b, represented by circles, and c, represented by crosses, against atomic weight for the five alkali metals: b varies irregularly, c smoothly.* (Proc. roy. Soc. *A*, **215**, 40, 1952.)

experiment. In fact, Born and Green say specifically 'No attempt will be made to obtain exact numerical values for physical constants, as this will require extended and tedious calculations.'

A different point of view is adopted by Eyring and his collaborators in a more specialized theoretical development [21]. They consider viscous flow as a type of chemical reaction, such as takes place in a gaseous reaction or in a dilute solution, which, at first sight at any rate, it would not appear to be. The assumption of 'holes' in the liquid plays an essential part in this work. Fürth likewise considers a liquid as containing holes, outside which is a continuum with the normal surface tension; the lifetime of the holes he regards as being governed by evaporation into them, a somewhat difficult assumption considering the size of the holes.

This is not the place to attempt any adequate consideration of these theories, to which so much ingenuity and such mathematical accomplishment have been variously devoted. The difficulty of establishing a theory of viscosity upon an unexceptionable physical and mathematical base being freely acknowledged, it may be said without disrespect that none of the elaborate investigations has led to any simple quantitative relation connecting viscosity with other constants and that, in view of its very wide validity, it seems unlikely that the temperature formulae (2) or (1) can be dependent upon the existence of central, spherically symmetrical forces between molecules in equilibrium. Some very general principle, widely independent of molecular species, must, it would appear, be involved.

VISCOSITY AND CHEMICAL CONSTITUTION

The use of the exponential formula (2), with two constants C and c, seems to offer a better opportunity of connecting viscosity with chemical constitution than the older methods in which viscosities at temperatures largely arbitrary had to be selected for comparison. The constant c represents an energy which should vary systematically within homologous series of organic compounds. As regards the melting-point viscosity, it has been already shown that, for monomolecular liquids:

$$\beta = \frac{\eta_M}{\alpha} = 5{\cdot}7 \times 10^{-4},$$

where $\alpha = (AT_M)^{\frac{1}{2}}\, V^{-\frac{2}{3}}$.

This is not to be expected to hold for any but monomolecular liquids, since it depends upon a formula for a fundamental frequency based upon very simple conceptions. At the same time it seems possible that the value of β—derived from the melting-point viscosity, the molecular weight A, and the molecular volume V—may be an important characteristic of the molecule. Methods of communication of momentum other than, and additional to, the vibrations of the molecule as a whole can only add to the viscosity, so that β should have the least value for monomolecular liquids. This is found to be so.

It has turned out that for certain molecules of similar structure and high symmetry the value of β is about the same [22]. Thus for CH_4, CCl_4, and $SiCl_4$, $\beta \times 10^4$ is about 20, and is nearly the same for $CHCl_3$ and $CHBr_3$. For the liquid halogens it is about 10. For molecules which depart greatly from central symmetry β increases rapidly and systematically with the asymmetry—for instance, in the case of the phenyl halides with increasing atomic weight of the halogens, and in the case of the paraffins with increasing number of carbons. In general, as has been mentioned, reliable values of melting-point viscosity are not available. It would be interesting to make a systematic examination of the values of β. It may be mentioned that for fused halides of the alkali metals, which should behave mechanically much as monomolecular liquids, the value of $\beta \times 10^4$ comes out as 6 if the average atomic weight of the two ions be taken for A.

It is found that, as far as measurements are available, the constant c varies systematically within homologous series. It is much to be desired that extended measurements with really pure organic substances should be made. Examples of the value of c, obtained by fitting formula (2) to Thorpe and Rodger's measurements, supplemented in certain cases, are shown: figure 4*a* gives c for some methyl, ethyl, and propyl esters and for certain double ethers. Figure 4*b* is for certain chlorides, bromides, and iodides. The regularity is clear and may suffice to indicate the chemical possibilities of a systematic study of liquid viscosities.

The quantity kc/v is an energy involved in the viscous transfer of momentum, derived on the assumption that this energy is proportional to $1/v$. Debye, assuming that the Van der Waals cohesion forces are due to polarization effects produced by one molecule on another, has shown that the energy E_F per molecule due to the intermolecular field is:

$$E_F = \frac{2}{NW}\frac{a}{v},$$

where W is the molecular weight.

It seems probable that the two energies may be closely connected [15], which means that c should be related to $a_0 = 2a/NWk$. Figure 5 shows c against a_0 for a collection of the typical organic liquids used by Thorpe and Rodger. It will be seen that, in general, there is a tolerable straight-line relationship, except for the alcohols, which are associated. It is clear that the effect of rising temperature will be to diminish association in these cases and thus to make the viscosity decrease abnormally, which means that c will be abnormally large, as observed.

Some years later Roseveare, Powell, and Eyring [21] showed that the energy $\Delta F^{\ddagger}$, the exponent in the viscosity-temperature formula being in their

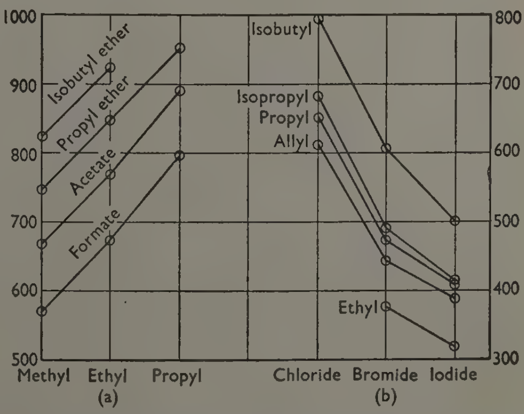

FIGURE 4 – *Variation of the constant c (plotted as ordinate) with chemical composition:* (a) *for certain esters and double ethers,* (b) *for certain halogen derivations.*

notation $\Delta F^{\ddagger}/RT$, stands in a roughly linear relation to the energy of vaporization ΔE for a collection of organic liquids (figure 6). The energy of vaporization includes, of course, an external work term. It has been shown that the ratio of the internal latent heat to the Van der Waals factor a/v is reasonably constant [15], so that this confirms the close connection between the viscous energy term and the potential energy of the molecule due to intermolecular forces in a liquid in equilibrium.

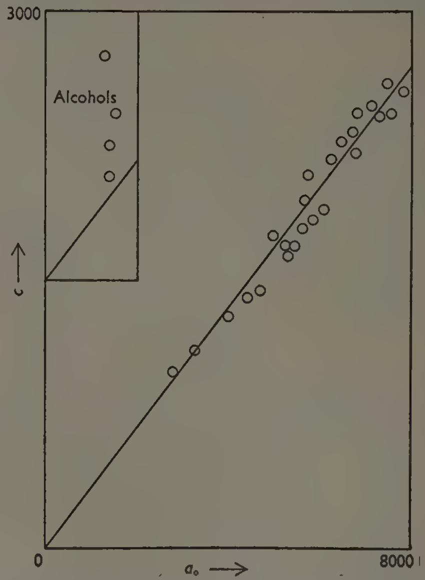

FIGURE 5 – *Viscous energy constant $c = E_{vis}\, v/k$ against $E_{mol}\, v/k$, when E_{mol} is the intermolecular energy due to Van der Waals forces.* (Phil. Mag., **17**, 719, 1934.)

EFFECT OF PRESSURE ON VISCOSITY

The work of Bridgman [9] has shown that the viscosity of all liquids[1] increases with pressure. For typical organic liquids the viscosity at 1000 atmospheres is two or three times the viscosity at normal pressure, but at the highest pressures the increase is very much more marked, the viscosity of isobutyl alcohol at 12 000 atmospheres, for instance, being 790 times normal. With mercury, the only monatomic liquid for which measurements are available, the effect is small, η at 20° C going nearly linearly from 0·0152 to 0·0201 when the pressure goes from 1 to 12 000 atmospheres. With water at temperatures below 30° the behaviour is, as noted, highly anomalous, but at 75° the viscosity steadily increases with pressure until at 9000 atmospheres it is 2·2 times normal, likewise an abnormally small effect.

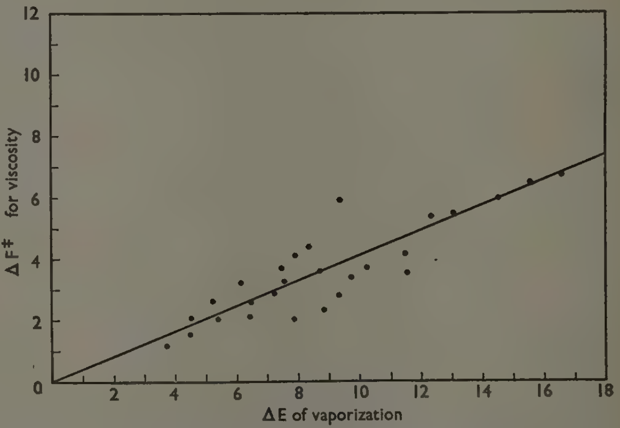

FIGURE 6 – *Eyring's* ΔF‡, ΔF‡/RT *being the exponent in the viscosity formula, against energy of vaporization* ΔE. (J. appl. Phys., **12**, 675, 1941.)

The simple theory allows us to make an estimate of the increase of viscosity with pressure [15]. The frequency of vibration at high pressure comes out to be:

$$\nu = GV^{\frac{1}{6}}\kappa^{-\frac{1}{2}},$$

where G is a constant, V the atomic volume, and κ the adiabatic compressibility, from which follows:

$$\frac{\eta_p}{\eta_1} = \left(\frac{V_1}{V_p}\right)^{\frac{1}{6}} \left(\frac{\kappa_1}{\kappa_p}\right)^{\frac{1}{2}} e^{\frac{C}{T}\left(\frac{1}{V_p}-\frac{1}{V_1}\right)} \quad \ldots .(5)$$

where suffix p denotes at high pressure and 1 denotes at one atmosphere. There are no data for adiabatic compressibility, but for liquids the ratio of the isothermal compressibilities will not differ much from the ratio of the adiabatic compressibilities and may be taken in its place.

With the only monatomic liquid available, mercury, formula (5) gives at 20° C for η_p/η_1, when $p = 12\,000$ atmospheres, the value 1·32, which is just the experimental value. As typical of the results with normal organic liquids we may take those exhibited in figure 7, where η_p/η_1 is shown against pressure for four liquids. In considering these results it must be borne in mind that in (5) there is no arbitrary constant available for adjustment, so that the agreement up to pressures of 2000 atmospheres is not bad. Above 2000 atmospheres the experimental η increases very rapidly,

[1] With the exception of water at temperatures below 30°. Water at these temperatures is, of course, very abnormal.

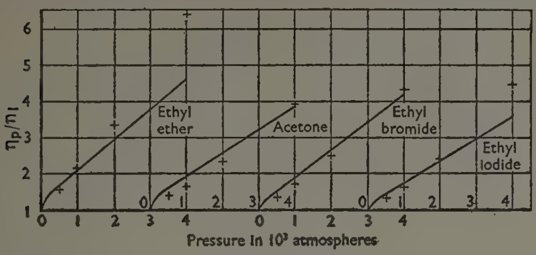

FIGURE 7 – *Relative viscosity η_p/η_1 against pressure. The curves shown are calculated from formula (5); the crosses are Bridgman's observed values.*

particularly so in the case of ether. Bridgman has shown that $(d^2v/dT^2)_p$ changes sign at a certain pressure, which is usually near 3000 atmospheres. This he puts down to the abolition of molecular interspace, higher pressures badly deforming the molecules. The formula, then, fails just when the conditions postulated are far from being fulfilled, and the departure is in the sense to be expected.

NEW EFFECTS WITH POLAR LIQUIDS

It has long been thought that an electric field might affect the viscosity of a liquid, and attempts to measure such an influence go back to König, who in 1885, with a crude apparatus, could detect no change of viscosity with carbon disulphide. A number of workers who devoted attention to the subject during the following fifty years or so agreed in finding no effect of an electric field on the viscosity of non-polar liquids, such as benzene and carbon tetrachloride, but recorded positive effects, of very varying magnitude, with polar liquids. With one and the same liquid different investigations yielded very discordant results, both as to the magnitude of the effect and its variation with field strength. In some cases increases of viscosity of 100 per cent, and even more, were recorded.

The problem was attacked again by Andrade and Dodd [23], who found that there was no change of viscosity to within 1 part in 100 000 with non-polar liquids, even with fields of 42 kV/cm, and further that all the large changes of viscosity recorded previously with polar liquids were spurious. All polar liquids conduct electricity to some extent, which leads to an accumulation of ions in the neighbourhood of the electrodes between which the liquid flows. These ions act as centres round which polar molecules cluster, leading to an increase of viscosity which is capricious, since it depends on the distance between the electrodes and other trivial factors. If, instead of a steady field, an alternating field is used, the effect decreases with increasing frequency until it becomes so small that it cannot be detected without special precautions.

If, however, very accurate methods of timing and very careful control of temperature are used, there is a small genuine increase of viscosity of polar liquids with field; this has to be measured with alternating fields of frequency in the region of 10 000 c/sec. It has been established that:

$$\frac{\Delta\eta}{\eta} = fF^2,$$

where $\Delta\eta$ is the increase of viscosity due to field, and f is a constant to which the name viscoelectric has been given. If the field is measured in e.s.u, f is in the neighbourhood of 2×10^{-7}. The smallness of the effect can be judged by the fact that, with the highest practicable field, the greatest value of $\Delta\eta/\eta$ is about 0·0012.

A general explanation of the effect can be found along the lines that any directional effect, such as that of the field, will tend to check the ordered rotation of the molecules which is a consequence of laminar flow. The present state of the theory of liquid viscosity does not allow a precise calculation of the effect, which remains for mathematicians to use as a touchstone for their theories.

Another new effect, established by Dodd and Hu Pak Mi [24], concerns the viscosity of supercooled liquids. Here again the effect has been established for polar liquids only. The nature of the effect is clear from figure 8, in which log η is plotted against $1/T$ for phenyl ether, which has the convenient melting-point of 26·85° C ($1/T_M = 0{\cdot}003335$). It will be seen that the plot is represented by two straight lines, intersecting at the melting-point. This is established beyond question by fitting a straight line to the points above the melting-point and then plotting deviations from this line, as shown in the inset. The melting-point found from the intersection is 26·95° C. The effect was established for other polar liquids, in particular by Hu Pak Mi for phenyl salicylate and menthol. It has since been found by Greenwood and Martin [25] for certain boron trifluoride compounds.

There is no measurable discontinuity of density at the melting-point, but Dodd and Roberts [26] have found with polar compounds a discontinuity in the variation of dielectric constant with temperature similar to that which exists for viscosity. The cause of the increase of viscosity has not been established, but it may possibly be attributed to the fluctuating formation of small, unstable

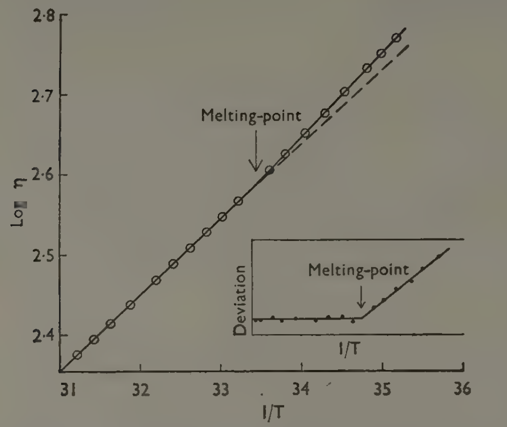

FIGURE 8 – *Log η against* 1/T *for phenyl ether in normal and supercooled states, showing discontinuity at melting-point.* (DODD and HU PAK MI. Proc. phys. Soc. *B*, **62**, 457.)

crystalline nuclei at temperatures below the melting-point. A careful study of the effect may throw light on the mechanism of melting.

Both the viscoelectric effect and the supercooling effect show for the first time that a difference between polar and non-polar liquids can be established by viscosity measurements.

NON-HOMOGENEOUS LIQUIDS

The class of suspensions known as lyophobic, or solution-hating, consists of liquids containing dispersed particles so small that they are kept from settling by Brownian motion. The pink gold sols are typical lyophobic suspensions, with the characteristic property that the addition of a very small amount of electrolyte will lead to irreversible coagulation. The viscosity of a suspension of spheres was worked out by Einstein on purely hydrodynamic grounds. He found that:

$$\eta = \eta_0(1 + 2{\cdot}5\varphi),$$

where η_0 is the viscosity of the pure liquid and φ is the total volume of the spheres in unit volume of liquid, which, surprisingly enough, is the only factor concerned in dilute suspensions of this kind. The formula has been extended for more concentrated suspensions by adding a term in φ^2. The properties of such suspensions are, then, explicable in terms of classical hydrodynamics, and their study does not in any way help to explain the nature of liquid viscosity.

The viscosity of suspensions of rod-like particles has attracted particular attention on account of the way in which Staudinger utilized it to find the molecular weight of high polymers. The mathematical problem was attacked by G. B. Jeffery, who substituted ellipsoids for Einstein's spheres and obtained Einstein's formula with, in place of the constant 2·5, a coefficient which was a function of the ratio $f = a/b$, where a and b are, respectively, the major and minor axes of the ellipsoid of rotation. Jeffery, like Einstein, did not take account of the Brownian motion. Eisenschitz [27] showed that different expressions involving the form factor f were involved in the case of Brownian motion and in that of no Brownian motion, but in both cases his formulae showed a viscosity proportional to the concentration. Experiment showed that this is not so except for small concentrations, and the longer the particles the smaller the limiting concentration for validity, which might be expected. At higher concentrations the viscosity increases much faster than the concentration, especially with very long particles. Staudinger assumed that the viscosity was proportional to the molecular weight for his dilute solutions of polymers, according to the formula:

$$\eta_s = \frac{\eta - \eta_0}{\eta_0} = KMc,$$

where M is molecular weight, c concentration, and K a constant characteristic of the polymer. J. M. Burgers [28] and others have criticized this assumption: it appears that there is a rough proportionality to molecular weight over a limiting range only, and that, in any case, the assumption of rod-like molecules cannot be valid for the suspensions concerned. The long molecules must be crumpled or coiled. The question is clearly a very complicated one, but Staudinger's investigations have brought it into prominence.

There are still more troublesome problems when we turn to the other class of suspensions, the lyophilic suspensions or gels. The exact definition of a gel is not a question on which we choose to linger. Typical of the class are dilute solutions of gelatine or agar. Whereas the lyophobic solutions are characterized by a Newtonian viscosity the lyophilic are not, the shearing stress increasing faster than the shearing strain. A further difficulty is presented by certain colloidal substances, of which paints are typical. Here the viscosity is a function not only of the rate of strain, but also of the previous history of the substance. A stirred paint—say a suspension of 30 per cent of lithopone in a liquid medium—flows freely if freshly stirred, but becomes progressively immobile on standing, although the state of easy flow

can always be restored by stirring. This is the familiar phenomenon of thixotropy, as Freundlich called it. With such substances we approach the difficulties that meet us when we have to consider the flow of the solid state. In general, the problems presented by the viscosity of suspensions, other than dilute ones of insoluble particles of simple shape, are very difficult, and many of them have not even been mentioned here.

CONCLUSION

The field of present-day research on liquid viscosity ranges, then, from the simplest monomolecular liquids, such as liquid sodium and argon, where the assumption of spherically symmetrical molecules can be justified, through more complicated monomolecular liquids, such as liquid gallium, where it undoubtedly can not, to a large class of liquids of varying molecular complexity, which all show Newtonian viscosity and are subject to a simple law of temperature variation. Among liquids of relatively simple molecular structure are abnormal liquids, such as water, where a varying association leads to peculiar difficulties. Suspensions extend the range of properties into fields of non-Newtonian viscosity, the more complicated ones leading us into regions where, as with solids, the flow properties are not solely determined by the temperature and pressure, but depend upon past history. Of certain fields, such as the viscosity of solutions, nothing has been said. From the theoretical point of view little has been done, except in the case of the simplest liquids, to account quantitatively for viscous properties or to connect them with other liquid characteristics. It would seem that the time is ripe for a new method of approach by such among the younger mathematical physicists as can muster interest in a very old problem, the liquid state.

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The Amsterdam Historical Medical-Pharmaceutical Museum

D. A. WITTOP KONING

Amsterdam is fortunate in possessing an authentic reconstruction of an early nineteenth-century pharmaceutical laboratory, fitted out with the actual contents of the original laboratory. This forms the nucleus of the Historical Medical-Pharmaceutical Museum, here described by the curator, Dr Wittop Koning. The Museum is particularly noted for its large collection of Delft-ware pharmacy pots, some of which are of great artistic merit.

With the decline of alchemy in the seventeenth and eighteenth centuries, practical chemical investigations tended to pass more and more into the hands of the apothecaries, many of whom were also physicians. In England, it is true, few of these pharmaceutical workers attained much eminence, though the names of George Starkey, George Wilson, John Quincy, and William Lewis are familiar to historians of chemistry. English chemistry of the time was advanced mostly by gifted amateurs, such as the leisured aristocrats Robert Boyle and Henry Cavendish, and the theologian and pamphleteer Joseph Priestley; the only professional British chemists of equal stature were John Dalton and Joseph Black. On the continent of Europe, however, the part played by apothecaries in the development of chemistry was considerable, as witness the names of Glauber, Lémery, Scheele, Sertürner, Pelletier, and Caventou.

Glauber (1604–70) was the first to describe the preparation of spirit of salt from salt and oil of vitriol; the sodium sulphate obtained in the same operation is still popularly known as Glauber's salt. He had an inkling of the relation between acids, bases, and salts, and foreshadowed later ideas on affinity and chemical bonds. Lémery (1645–1715), court apothecary to Louis XIV of France, wrote a celebrated text-book of practical chemistry, *Cours de Chimie*, which was first published in 1675 and afterwards appeared in many editions and in many languages. Scheele (1742–86), a Swedish apothecary, discovered oxygen, chlorine, hydrogen fluoride, glycerol, and numerous organic acids. Sertürner (1783–1841) discovered morphine, which he isolated from opium; Pelletier (1788–1842) and Caventou (1785–1878) discovered quinine, strychnine, brucine, and cinchonine, and in 1819 invented the word chlorophyll.

To this list of apothecary-chemists many other names could be added, but those mentioned are sufficient to show how largely chemistry was indebted to the pharmaceutical laboratory in the period immediately preceding the birth of the modern science. It is therefore a matter of much interest that practically the whole of the contents of an early nineteenth-century Dutch apothecary's laboratory has been preserved and is now housed at Amsterdam in a reconstruction of the laboratory itself. This forms one of the exhibits in the Historical Medical-Pharmaceutical Museum in the Guildhall of the Vintners, the only one of the original guildhalls of Amsterdam to survive.

The pharmacist was Anthoni d'Ailly (1766–1825), who took over from T. P. Schonk a laboratory that had been established in 1776. He soon began to produce numerous drugs on a manufacturing scale, and we owe the preservation of his laboratory to the fact that from it grew a flourishing business in chemicals and pharmaceuticals still in existence. d'Ailly's grandson, indeed, assisted C. E. Daniëls, the founder of the Museum, to arrange the pharmaceutical section. The reconstruction of the laboratory in 1902 was given verisimilitude by careful reference to two water-colours of it (one is reproduced in figure 2) painted in 1818 by J. Jelgerhuis; noteworthy are the beautiful panelled ceiling and the masonry furnace, which capture the atmosphere of the period. It may be added that the reconstruction and arrangement of the laboratory have been so carefully carried out that it is more than a museum piece: if necessary, practical operations could be started in it at any moment without further preparation.

Anthoni d'Ailly's empty right sleeve (figure 1) is witness to the fact that he was an experimenter: on 17th January 1809 he lost an arm through an explosion of silver fulminate. However, he soon

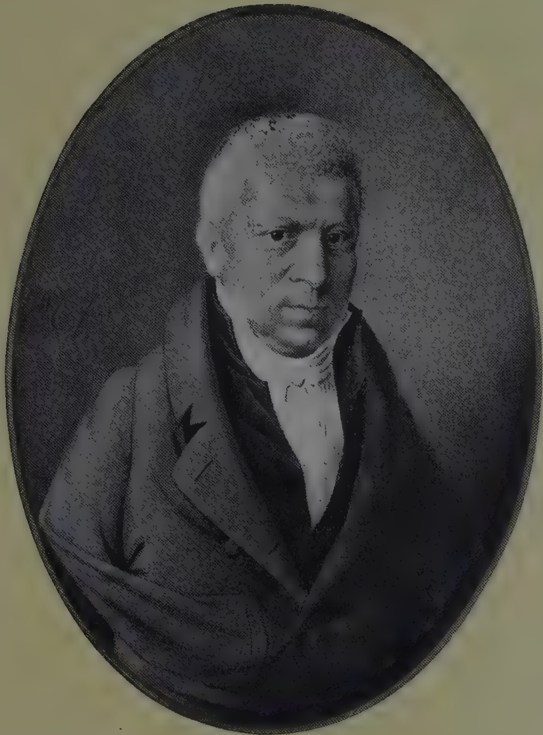

FIGURE 1 – *Anthoni d'Ailly.*

FIGURE 2 – *Water-colour painting of d'Ailly's laboratory, by J. Jelgerhuis.*

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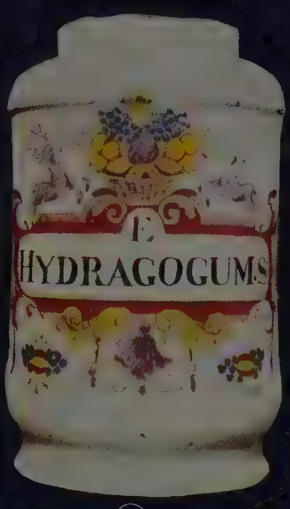

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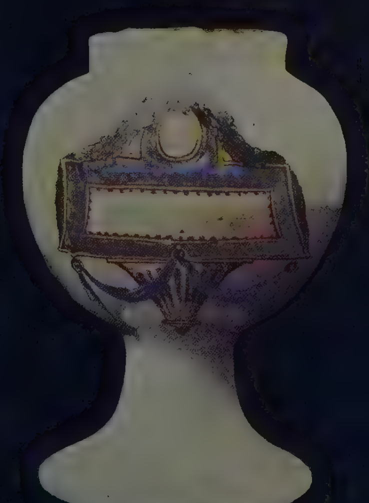
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FIGURE 10 – *A mortar cast by Conradus Splinter in 1645.*

became primarily a business man, and a ledger covering the years 1819 and 1820 gives information about his considerable output and numerous clients; from this ledger the author compiled a price-list of d'Ailly's products and the quantities that he sold during these years. The data are important for the study of the cost of pharmaceuticals, an illuminating aspect of the history of pharmacy that has received close attention in Germany.

After d'Ailly's death, his two sons continued the business, and one of them, A. J. d'Ailly (1793-1851), became well known for his scientific work. He was, for example, the first apothecary to become a member of the commission for the Dutch Pharmacopoeia, and helped to compile the 1851 edition; all the other members of the commission were physicians. Anthoni's son-in-law, also a partner in the firm, was the first to prepare quinine from Javanese cinchona, and thus secured for Amsterdam the market in the Javanese bark.

Of the objects in the laboratory, perhaps the most outstanding is a large plate of Chinese porcelain used for the evaporation of extracts. This use may seem a strange one, but porcelain is exposed to much higher temperatures during manufacture than is common pottery and is thus better suited for withstanding heat when used for inspissation. The balances in the laboratory are of interest; one of them contains a number of seals that have allowed the reconstruction of the series of year-seals of the Dutch inspectors of weights and measures [1].

Besides the laboratory there is a pharmacy (figure 3) with Louis XVI panels, acquired by the Museum from another pharmacy now demolished. This panelling admirably sets off the large collection of Delft-blue pharmacy pots, which is the finest in the world and particularly interesting for its great variety in designs and potters' marks. The name Delft-ware is given to pottery covered internally and externally with a layer of tin glaze, in contrast to the older majolica which has a transparent lead glaze; it is made not only at Delft but, for example, at Lambeth (London) and in France and Belgium.

Besides the Delft-blue pots in the Museum there are some polychrome specimens; these deserve special attention, as they are very scarce (figures 4–9). Figure 4 shows a cylindrical pot with the inscription E HYDRAGOGUM. S.; it is decorated with a variant of the famous peacock motif, showing deer instead of peacocks, and is unmarked. Figure 5 is of a cylindrical pot belonging to a series of three. It is inscribed E LENITIV: L: and

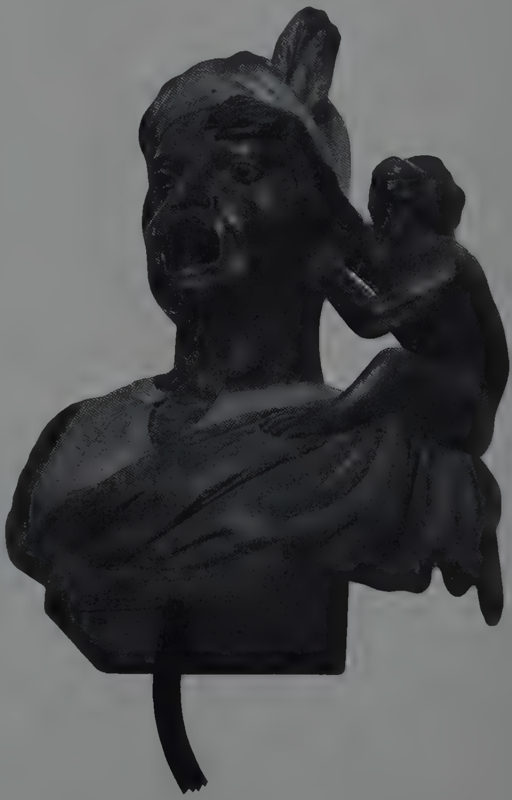

FIGURE 11 – *A 'gaper', or sign of an apothecary's shop.*

is decorated with a reclining deer between two aloes. It bears no potter's mark. Figure 6 shows a syrup jug with the inscription S CERAS : NIGR; it is decorated with a flower motif with a plant over it. It is marked with a symbol of three bells. Figure 7 is another syrup jug inscribed S RUBI JDEI. It is unmarked, and is decorated with two figures of naked women with banderoles; in the middle is a flower motif. Figure 8 illustrates a third syrup jug, one of a series of four; it is decorated with a console motif but has no inscription. It is marked lpk, i.e. De Lampetkan. Figure 9 shows a cylindrical pot inscribed AXUNG: OXŸGENAT; it is decorated with a leaping stag and is marked with three bells.

The Museum possesses many apothecaries' mortars [2], one of which was cast by Segewyn Hatiseren and is dated 1531; another mortar by the same maker, dated 1540 and in much better condition, is in the Victoria and Albert Museum, London. A second mortar is that cast by Conradus Splinter in 1645 (figure 10); the only other known specimen by this maker is also in the Victoria and Albert Museum. Holland and Belgium are famous for the mortars cast there, principally at Deventer and Malines; they were made not only for pharmaceutical use but for household purposes, and were often given as wedding presents—hence such legends as *Amor vincit omnia* or its Dutch equivalent *Liefde verwint al dinc*. Mortars were also fashioned from materials other than metal—for example, marble, serpentine, wood, and glass. The Museum possesses specimens of all these varieties, as well as one of ivory.

Mention may also be made of the typically Dutch 'gaper,' which served as a signboard for a pharmacy. There are several of these in the Museum; one, with a monkey on the shoulder, is shown in figure 11.

In an upper room of the Museum are displayed medical instruments, books, and pharmaceutical objects not belonging directly to the laboratory. There are also portraits of famous physicians and apothecaries, such as Boerhaave and Vesalius, Seba and Abraham Francen. Seba is remembered for his cabinet of natural curiosities, which he sold to the Czar of Russia. In Amsterdam, then the largest commercial city of continental Europe, it was not difficult to assemble strange and curious exotic objects; the sailors brought back such things from various parts of the world and apothecaries were always ready to experiment with new plants, drugs, poisons, and the like. Commerce affected apothecaries in another way also, for the East Indiamen and other ships had to be supplied with medicines for the voyage and for the colonies. Some of the medicine-chests made and fitted out for this purpose have survived, and three of those used on board merchant ships are now in the Museum.

Until the French domination of the Low Countries by Napoleon, the education of apothecaries took place in pharmaceutical practice only; candidates were examined by the guilds of apothecaries or the *Collegia Medica* and were not allowed to present themselves without a written certificate of practical experience. Some of these certificates, as well as diplomas granted to successful candidates, are preserved in the Museum. During their training, students used chests of simples containing specimens of all those drugs which they were expected to be able to identify at sight. The Museum possesses a beautiful example of such chests; it contains some hundreds of simples, many of which are no longer in use.

Those who wished to make themselves acquainted with living medicinal herbs had recourse to the *Hortus Medicus*, which issued free admission tokens to physicians, apothecaries, surgeons, and students. There are several of these tokens in the Museum, as well as guild medals awarded by the Guild of Apothecaries as a token of membership.

Lastly, we may recall that Fahrenheit worked in Amsterdam for the greater part of his life, making not only thermometers but hydrometers. At that time, the difficulty was to establish a fixed hydrometric scale for such instruments, and apothecaries were therefore advised in the Amsterdam pharmacopoeia to buy their hydrometers from one firm only. All the instruments made by this firm were signed, and one of them, made by Fahrenheit, is not the least of the treasures possessed by the Museum.

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Science and chronometry

ADRIEN JAQUEROD

Astronomers, physicists, and mathematicians, including some of the most celebrated among them, have been absorbedly interested in the measurement of time throughout the whole of history. For them it is often the essential independent variable, to be measured with the greatest possible exactitude. Professor Jaquerod here discusses recent developments in chronometry, a branch of science to which he has himself made notable contributions.

In order to measure time, it must be subdivided into equal portions of suitable size; for this, some periodic process must be discovered that has a constant period independent of internal or external factors, a fact which can be checked only by comparison with other periodic processes quite distinct from the one selected.

Over a period of centuries experiments were made with well known instruments: gnomons, clepsydras, sand-glasses, and the like. From the seventeenth century onward, more and more use came to be made of the gravity pendulum, proposed by Galileo and realized first by Huygens, and of the balance-wheel coupled to the spiral spring, also conceived and realized by Huygens. Hooke [1] made an important contribution to this phase of chronometry by discovering the law known by his name, which he enunciated in Latin as *Ut tensio, sic vis*; in modern terms, the elastic deformation is proportional to the force producing it. If this law were rigorously accurate, as was believed for a long time, the free oscillations of an elastic system would be isochronous; that is to say, their period would be independent of their amplitude.

The use of the pendulum and the spiral spring constituted an immense step forward. Up to that time, watches and clocks had been regulated—very roughly—by a verge, that is, a sort of balance-rod or ring executing a to-and-fro movement under the influence of some motive force (weight, spring) acting through an escapement (verge escapement). The period of the movement varied enormously, especially as the tension diminished, and a watch which did not vary by more than a quarter of an hour a day was a marvel. These variations arose mainly because the verge has no proper period, owing to the absence of any couple tending to bring it back to a position of stable equilibrium.

It is a curious fact that Galileo believed in the strict isochronism of the pendulum; Huygens soon saw that this was illusory, and that the period increases with the amplitude. He sought to eliminate this failing by a device in which the pendulum was suspended from a flexible wire or ribbon, making contact on each side, as the pendulum oscillated, with metal cheeks of cycloidal shape. He showed mathematically that the oscillations of this pendulum should be isochronous. However, he had nothing but disappointment with it—for reasons which it would take too long to explain here—and abandoned the idea [1].

It was also appreciated fairly quickly that even the oscillations regulated by the balance-wheel and spiral-spring system are not isochronous when they are governed by means of an escapement. Precision of measurement has increased with technical progress, and as early as Huygens' day the effect of temperature on the spiral spring was noted; watches and clocks run slow when the temperature rises.

It can with truth be said that the greatest efforts of the last three hundred years were and still are directed to the elimination of these causes of error: deviations from isochronism and the effect of temperature. These efforts have been so successful that today the best astronomical clocks do not vary, on the average, by more than a hundredth of a second per day, and sometimes the variation may be only a few thousandths; there are watches which vary by only a few tenths of a second. Let us see how these remarkable results have been achieved.

(*i*) *The pendulum.* The numerous attempts to make the pendulum isochronous have all been fruitless, and even today the only method of ensuring constancy of period is to keep the amplitude constant—a makeshift solution. The necessity of controlling the oscillations, by means of an escapement, exerts a considerable effect on the isochronism, and the aim has been to reduce this

effect to a minimum. Shortt's clock with a so-called 'free' pendulum gives a remarkable performance in this respect.

On the other hand, compensation, i.e. elimination of the effect of temperature, has been achieved with a high degree of accuracy. Graham (1715) was the first to construct a compensated pendulum —the mercury pendulum. Here the rod is of steel, carrying a mercury container whose thermal expansion raises the centre of oscillation and thus compensates for the expansion of the rod, which tends to lower it. Later (1726), John Harrison conceived the familiar grid pendulum, but the most important advance was made much more recently by C. E. Guillaume [2], who investigated the anomalies in the coefficients of expansion of nickel steels. These coefficients, when plotted against nickel content, give a curve with a very sharp minimum at 36 per cent Ni, where the coefficient of thermal expansion is almost zero. The alloy of this composition is called Invar, and is widely used in metrology. A pendulum with an Invar rod has an almost constant length; the very small residual expansion can be compensated by the expansion of the bob.

Unfortunately, nickel steels are unstable: their dimensions change slowly with time, causing a variation in the rate of the clock-mechanism. This can be eliminated by a suitable thermal treatment, and, as Guillaume showed, by the inclusion of chromium in the alloy. Nowadays the majority of precision clocks have pendulum rods of Invar.

The effects on the period exerted by the ambient air have also been much studied, e.g. by Stokes and Bessel. There are several such effects, one of which is a damping, causing a slight change in the period. But the most important effect is the action of the air in virtue of Archimedes' principle: it produces an upthrust, whence an apparent diminution in the weight, that is, in the restoring force. Finally, air which is carried with the bob increases its apparent mass. Variations of barometric pressure and temperature make themselves felt, by varying the density of the air. Methods of compensating for them have been sought, for instance by combining a mercury barometer with the pendulum. This procedure has been abandoned, and the modern method of eliminating the influence of pressure-variations is to place the clock in an enclosure in which the pressure and the temperature remain constant. All astronomical clocks are so enclosed.

(*ii*) *Balance-wheel and spiral-spring* (*watches*). Ever since the invention of the balance-wheel and spiral-spring system, the makers of chronometers, and many scientists, have paid much attention to improving the compensation and the isochronism of time-keeping mechanisms, for the defects, particularly as regards compensation, soon became obvious. These studies were stimulated by a prize of £20 000 offered in 1714 by the British Government to anyone who should solve the problem of the determination of longitude at sea—that is, of constructing a chronometer which would give reliable service under sea-going conditions. After a long delay, the prize was awarded to Harrison in 1773 for his marine clock, in which the bi-metallic balance-wheel, which compensated for the effect of temperature on the spiral, played an essential part.

Early in the present century, Guillaume [3] produced an entirely different solution. Instead of compensating for the effect of temperature by exerting an opposed effect on the balance-wheel, he eliminated it in the following manner. A Swiss maker of chronometers observed an unexpected temperature-effect in a watch having an Invar spring. Guillaume made a systematic study of the phenomenon, and discovered that the plot of Young's modulus against temperature for an alloy containing approximately 42 per cent of Ni passes through a maximum and minimum, instead of following a uniform, linear course like that for steel. At these points the thermoelastic coefficient is zero. He then found that addition of 12 per cent of chromium yielded an alloy which, in the region of normal operating temperatures, had a modulus that does not vary with temperature. This alloy is called Elinvar. A spring made of this alloy is said, not altogether correctly, to be auto-compensated. At the present day there are many such alloys—Metélinvar, Nivarox, Isoval, etc.—and the use of a steel spring and bi-metallic balance mechanism has been practically abandoned, except for marine chronometers and watches of the highest precision.

A theoretical attack on the problem of isochronism was begun during the last century. Phillips [4] made an essential contribution: he showed that the geometry of the spiral must conform to rigorous laws, and particularly so the form of the terminal curves. Phillips' theory has been simplified and developed further during the present century by Keelhoff and, above all, by Haag [5].

All these mathematical theories assume a material obeying Hooke's law. The present writer has studied this point experimentally, using both torsional and flexural tests, and has shown that

isochronism is never, or hardly ever, realized, even in a free system at very low amplitudes, the limiting case in which it is assumed to occur. What is more, variations in period are generally the more rapid the smaller the amplitude. Mechanisms constructed from the majority of metals and alloys exhibit these deviations from isochronism, sometimes considerable and often varying with amplitude in a curious manner. This behaviour can be modified in various ways by thermal and mechanical treatments. Among metallic substances, certain alloys of copper, such as cupro-beryllium, yield mechanisms whose isochronism is remarkable at very low amplitudes. On the other hand, glasses have excellent isochronism, with deviations 1/30–1/100th of those for steel. Efforts should be made to use them in precise chronometry, for they would offer many advantages [6].

In any case, chronometry has now reached a turning-point and, although the pendulum and the balance-wheel and spiral-spring can look forward to continued application for everyday measurement of time, they are both almost certain to be ousted for high-accuracy measurements by the tuning-fork clock, and especially by the quartz-crystal clock and that described as molecular or atomic. The general principle is the same in each case, namely to use an oscillatory motion for subdividing time into equal fractions, and the difficulties to be overcome are essentially the same as in classical chronometry.

A tuning-fork executes practically isochronous vibrations. These can be maintained by a circuit (figure 1) containing a triode and two small polarized electromagnets. The sinusoidal current from this circuit is fed to a synchronous motor and clockwork mechanism. Attempts are made to keep the amplitude constant and, to prevent variations of frequency arising from variations of temperature, the fork is made of Elinvar. The error is of the order of 10^{-4} per cent, or 1/10th of a second per day. It is difficult to reduce it further.

The quartz clock [7] utilizes the elastic vibrations of a quartz rod, ring ('doughnut'), or plate maintained by an oscillating electrical circuit, thanks to the piezoelectrical properties of quartz.

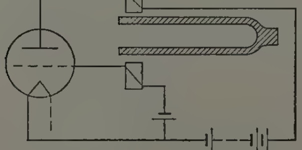


FIGURE 1

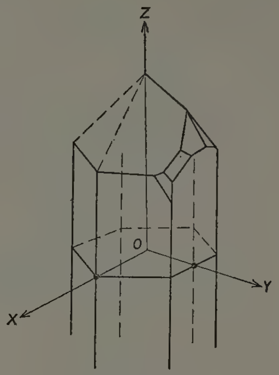


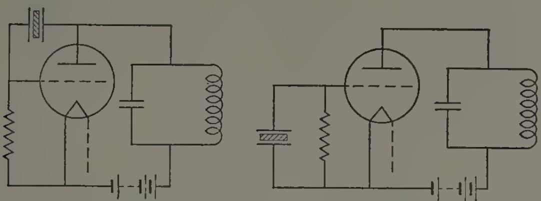
FIGURE 2

Piezoelectricity was discovered in 1880 by Pierre and Jacques Curie [8]; its essentials, as far as they interest us here, are as follows.

Figure 2 is a sketch of a quartz crystal with three rectangular reference axes. OZ is the crystallographic or optical axis, OX the electrical axis. Let us describe within the crystal a regular parallelopiped. If a pair of specially well developed faces is perpendicular to the OX axis, the parallelopiped is said to be produced by an X-cut, and so on. Oblique cuts are also of interest, as we shall see.

Let us consider such a parallelopiped parallel to the three axes. A pressure exerted along OX or OY produces two electrical charges of opposite sign on the faces perpendicular to OX, proportional to the pressure. A tensile force along OY produces opposite charges. This is the direct piezoelectrical effect. The inverse effect, predicted by Lippmann in 1881, is the production of an expansion or contraction along OX or OY, but not along OZ, by an electrical field acting along (or against) the direction of OX. If the quartz crystal is placed in an oscillating field, e.g. a sinusoidal one parallel to OX, it will be set in forced vibrations, which will attain maximum amplitude at resonance, i.e. when the frequency of the oscillating field is exactly equal to the natural frequency of elastic vibrations (number of oscillations per second) of the crystal. This crystal then imposes its natural frequency on the circuit.

Figure 3 shows the simplest arrangements (Pierce, and Pierce-Miller, oscillators) for maintaining these oscillations in a way suitable for controlling a chronometer. The frequency of vibration, which depends on the size of the crystal, is of the order of 100 000 cycles per second—much too large to be used directly. An electronic



Pierce oscillator

Pierce-Miller oscillator

FIGURE 3

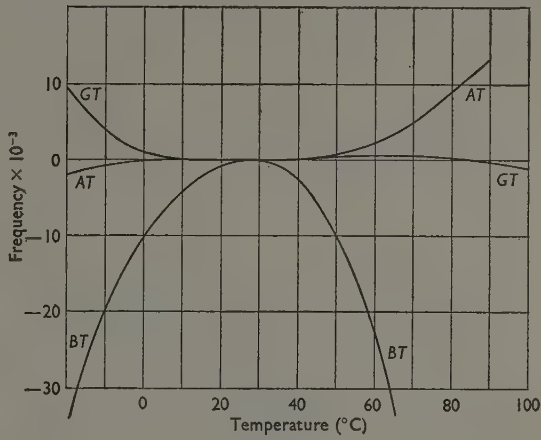


FIGURE 5

device 'demultiplies' this frequency, that is, lowers it successively to 1/2, 1/5, or 1/10th of its value, and finally to a frequency of say 1000 or 100, suitable for operating a synchronous motor which rotates with the same regularity as the vibrations of the controlling quartz, and can move the hands of an appropriate clockwork mechanism.

This regularity depends on two factors: isochronism of the quartz vibrations, and variations in temperature. Since the quartz crystal is part of a condenser which is itself part of an oscillatory electrical circuit on which it imposes its natural frequency, the amplitude of the vibrations will be a function of the power-input. If this power is plotted along abscissae against frequency as ordinates, a curve similar to that for cupro-beryllium is obtained. Since there are difficulties in driving the crystal at the very low power at which oscillations are strictly isochronous, there is a certain deviation from isochronism; this is countered—as for a clock with a gravity pendulum—by striving to maintain the power-input at a constant value.

To deal with effects due to temperature-variations is a complex problem. If the crystal has the form of a plate and executes longitudinal vibrations along OY, a strongly negative thermoelastic coefficient is encountered. This coefficient can be made positive by changing the direction of the cut, and the vibrations then follow a complicated pattern. An orientation of the cut is sought such that the frequency/temperature curve exhibits either a maximum ($dn/dT =$ zero) or a point of inflexion to which a horizontal tangent can be drawn. Figure 4 shows two cuts which are used, and figure 5 their frequency/temperature characteristics. The GT cut, much used for high-precision quartz clocks, is not shown in figure 4; however, figure 5 shows that, for this cut, the effect of temperature on frequency is practically zero between 0 and 100° C [9]. The quartz ring or 'doughnut' is excellent but requires careful handling, especially when mounting it. In any case, the temperature of the crystal must always be maintained constant to within a few thousandths of a degree by thermostatic control: this is no simple matter.

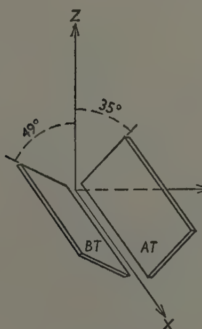


FIGURE 4

How accurate are the best quartz clocks? For comparison, it may be recalled that good astronomical pendulum clocks, particularly those with Shortt pendulums, keep time to within a few thousandths of a second per day, a deviation of 2–3 × 10^{-8}. The error of the best quartz clocks is not greater than 10^{-9}, or 1/10 000th second per day, i.e. the deviation of such a clock is less than 1/10th of that of a good astronomical clock. It is obvious that comparison can no longer be made against sidereal time determined from the rotation of the Earth. For one thing, there is an uncertainty in the astronomical determination of this time of 0·01–0·02 sec, and for another, as will be seen below, the sidereal day is not an absolutely constant quantity, but suffers from variations that cannot be tolerated in chronometry. The accuracy of time-keeping by various clocks can be determined only by intercomparisons. The main observatories keep several of them (eighteen at

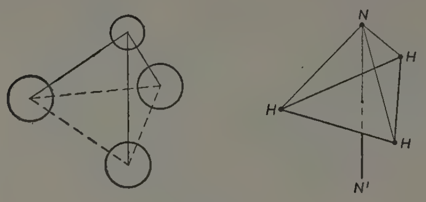


FIGURE 6

Greenwich, for instance, piloted by quartz rings).

Does the quartz clock suffer from any disadvantages which offset the enormous advantage of its high precision? It would, indeed, be surprising if it did not. The main trouble is the drift in frequency which is observed in the first years of running, generally a very slow acceleration tending asymptotically towards constancy. This ageing is suffered by a quartz crystal even in very high vacuum, and arises from various causes still little understood: evaporation of the electrodes deposited on the crystal by sublimation, adsorption of gases, changes in the structure of the quartz itself.

In addition, the electronic equipment of these clocks is subject to irritating breakdowns due to the multiplicity of valves, condensers, and so on. When the system is started up again after any stoppage, it only slowly settles down to operation at its initial rate. Is it possible to eliminate all these inconveniences? Great hopes are placed in the molecular or atomic clock. This is a time-keeper controlled by a truly constant oscillation, completely independent of external conditions. It can be assumed that the internal vibrations of any molecule, or atom, fulfil this condition absolutely. The ammonia molecule, NH_3, for example, has the structure shown in figure 6—a pyramid on an equilateral triangular base, with the nitrogen atom at the summit. This atom can vibrate between the two positions N and N′, emitting an electro-magnetic radiation of frequency 23 870 Mc/s, with a wavelength of 1·2658 cm, very far in the infra-red. The molecule can be set in vibration by radiation of the same wavelength, which is consequently absorbed. The resonance curve has a sharp maximum. A long (10 m) tube, serving as a guide for a wave of suitable frequency, and filled with gaseous ammonia, will transmit radiation without or with attenuation according as the frequency of this radiation is exactly equal to, or slightly less than, 23 870 Mc/s.

At the moment of resonance there will be a definite signal from this tube, which can be adapted for regulating a timepiece, such as an ordinary quartz clock. This is the principle of the molecular clock, constructed by H. Lyons at the National Bureau of Standards, Washington [10]. Unfortunately, it has hitherto functioned only intermittently, the main difficulty having arisen from variations in the very low pressure of ammonia in the tube due to various causes, notably adsorption. However, there are reasons to suppose that it will be possible to surmount this difficulty, particularly by using an isotope of a heavy element—caesium, for example—and that timepieces may be constructed with a much higher precision than that previously achieved by other methods.

To conclude, let us see of what value the Earth is as a clock. Up to the present—though it will not be so in the future—the mean solar day has been taken as the unit of time. This depends essentially on the angular velocity of rotation of the Earth, making allowance for its translation round the Sun. Exact information about the determination of the length of the hour will be found in an article by Sir Harold Spencer Jones [11], at the end of which he says 'A new era of time-measurement has arrived, and clocks made by man now hold out a distinct promise of being able to convict the Earth of irregularities in time-keeping.'

Some considerable time ago, indeed, scientists first supposed, then proved and calculated, that the tidal friction between oceans and crust is gradually diminishing the angular velocity of the Earth. The effect is extremely small—one or two thousandths of a second per day in a century—and there is no immediate hope of directly demonstrating it experimentally. Experiment has, however, revealed something else, which was not predicted (though it was envisaged by Newton) and which astronomers and geophysicists are now studying with great interest, namely variations in the angular velocity, ω, of the Earth around its mean value, which is practically constant. Apart from the effect of tides, the angular momentum of the Earth, $I\omega$ (I = terrestrial moment of inertia), is constant. If for any reason I should vary, ω would vary correspondingly. I depends on the total mass of the Earth and its distribution around its axis of rotation. Thus any transposition of mass in the Earth will produce in general a change of angular velocity. When a man travels towards the equator, he lengthens the day; when he travels away from it, he shortens it. Of course the effect is insignificant, but if considerable masses are displaced (e.g. of air, or of water to the equator

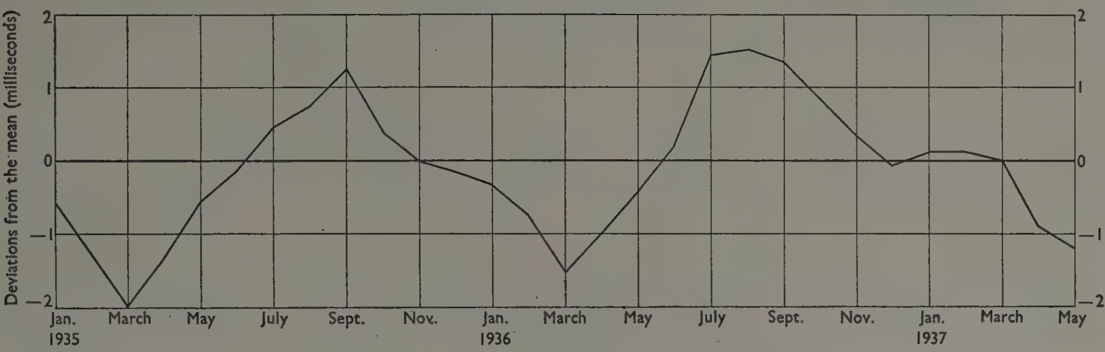


FIGURE 7

through melting of the polar ice-cap, by outpourings of molten lava, by the raising up of continents, etc.), the variations in the length of the day might become appreciable. If this were to happen, a disagreement between sidereal and clock time would occur: clocks would appear to gain or lose.

Astronomers have for some long time observed irregularities in the movement of the Moon (which also serves as a clock) for which there has been no theoretical explanation. Similar and parallel irregularities have been observed in the motions of the planets. There can be only one explanation: the Earth is at fault.

In 1937 Stoyko [12] published records of the running of a series of astronomical clocks at the Paris, Washington, and Charlottenburg observatories, which vary in parallel with one another. Figure 7 shows the results for the period 1st January 1935 to 30th April 1937: the mean monthly deviations, in thousandths of a second per day, are plotted along the ordinates, and the times of observation along the abscissae. A thousandth of a second per day may be small, but in a month it adds up to three hundredths—quite a perceptible amount. The graph shows that there is an annual periodicity among the variations.

These variations of angular velocity are very apparent with quartz clocks, whose accuracy (as already stated) is at least ten times as great as that of ordinary astronomical clocks; and there will soon be some hundreds of these quartz clocks distributed over the two hemispheres. It is already known that there is an annual periodicity in the terrestrial fluctuations, as well as a semi-annual one, and that there are also fortuitous changes which sometimes occur quite suddenly. Close study of these arresting facts, which will need international collaboration, and the efforts made to define their causes, will certainly lead to a more exact knowledge of several interesting phenomena in geology and geophysics. One is even justified in hoping for important discoveries, perhaps sensational ones, which will compensate us for having to give up the Earth as a time standard.

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Some scientific investigations at the National Gallery, London

F. I. G. RAWLINS and A. E. A. WERNER

The methods described in this article are the result of closely co-operative teamwork. The authors wish to emphasize the leading parts taken by Miss R. J. Plesters, Mr J. S. Mills, and Mr I. Graham. In particular, the development of microtechniques has progressed under the stimulus of the Conservation Department, and has now become routine practice. The Nuffield Foundation has made possible the long-term researches in chemical physics.

Previous communications to ENDEAVOUR [1, 2] have described the general principles underlying the application of scientific methods to the problems of conservation. It is now proposed to discuss in some detail processes that have been developed during the last few years. These cover some of the routine work in which the laboratory supports the restorers' studio, but in addition there is now the programme brought into being as a result of the Nuffield Foundation's generous grant for long-term research.

We are not concerned with the compilation of records; what is involved at this stage is a conspectus of tasks undertaken to learn about the special way in which the various components of a painting are physically related to one another. Alongside has gone the first attempt to apply chromatographic methods to the elucidation of the chemistry of the natural resins, and to their detection in paint media. In addition, a study is being made of the mechanism involved in the diffusion of solvents through linoxyn films.

It will be observed that the approach in all these cases is towards a physico-chemical study of the behaviour of the substances from which 'classical' paintings are normally constructed.

MICRO-SECTIONS OF PAINT SAMPLES

Although painting-techniques may have differed through the ages—modern methods being usually simpler—there is, broadly speaking, one basic principle underlying them all, namely that a painting is a stratified object. This layer-like structure is essentially fourfold, and (starting from the back) it comprises (i) the support, (ii) the ground (or gesso), (iii) the paint layers proper, and (iv) the protective coating (or varnish).

Since a knowledge of the stratified structure of a painting is frequently of interest to the restorer, and also can provide valuable information about the methods used by the old masters in building up their paintings, a method for mounting minute fragments of paint for a microscopical study of the layers in cross-section has been developed. The technique is similar to that employed in the preparation of cross-sections of metals or minerals. The paint-fragment is embedded in a suitable mounting medium, ground with emery papers of increasing degrees of fineness, and given a final polish on a buffing wheel. The primary question is the choice of a suitable mounting medium. In the past, attempts were first made with mixtures of paraffin wax and ceresine, but they were not very successful. The mounting medium was too soft, and during the grinding (or cutting) there was a danger of fracturing the paint-fragment. A method using polymethyl-methacrylat resin (Perspex) as the mounting medium was introduced to overcome this difficulty.

However, the material that offers the best possibilities as an embedding medium is the polyester resin marketed under the trade name Marco Resin 26 C, which has already found considerable use in museum work for the embedding of comparatively large specimens [3]. Polyester resins with similar properties are also marketed for this purpose as Ceemar Resin and Beetle Resin 4116. The advantages displayed by these polyester resins as embedding media are briefly as follows: (i) they are cold-setting, thus eliminating even a theoretical risk of damaging the paint-fragment by heat; (ii) the prepolymer is a mobile liquid which easily penetrates the paint-fragment, and also permits air-bubbles to be dispersed without difficulty; (iii) they are water-white and have a refractive index (*c* 1·5) approximating to that of Canada balsam; and (iv) when set they are almost unaffected by acids, alkalis, and organic

solvents, except upon prolonged exposure. Furthermore, since it is not necessary to apply pressure during setting, the mounting can be carried out in a flexible polythene mould, from which the solid block of resin can easily be ejected by pressing the sides. 'Flexicubes,' sold for making ice-cubes in refrigerators, have been found most convenient for this purpose.

The optical examination of the cross-section reveals the arrangement of the layers, and their appearance often gives a clue to the type of pigment present. This is normally confirmed by a chemical analysis of an unmounted paint-fragment from the same area of the picture, using the modern organic reagents for metals in conjunction with Feigl's spot-test technique. However, in favourable circumstances it is possible to carry out microchemical tests on the actual cross-section. Thus the presence of white lead in a paint-layer can be readily shown by the formation of a bright yellow colour when the cross-section is treated with a drop of dilute hydrochloric acid followed by a drop of potassium iodide solution. Similarly the presence of iron pigments can be revealed by the Prussian blue test. The chemical reagents do not penetrate the paint-fragment; if it is sufficiently thick, it can be reground so as to expose a fresh surface, upon which further chemical reactions may be carried out. This development is proving of great value for the identification of pigments present in individual layers of paint, since in the majority of cases it is not possible to obtain samples of the separate paint-layers for examination.

As the dates of the discovery of very many pigments are known with some accuracy, this knowledge can be used in certain circumstances to determine the earliest date at which a picture could have been painted, and thus perhaps to expose faulty or fraudulent ascriptions. Two such instances occurred recently during a review of paintings in the National Gallery. Specimens of blue and green *original* paint (in taking specimens for analysis, care must naturally be exercised that the area from which the specimen is taken is original paint and not an area of later repaint) from a picture ascribed to the seventeenth-century Dutch school were found to contain Prussian blue and opaque chromium oxide respectively. Prussian blue was first used in Holland in the second half of the eighteenth century, and chromium oxide was not in common use as an artists' pigment until about the middle of the nineteenth century. The second example concerned a painting ascribed to Murillo: a specimen of original blue paint was found to contain cobalt blue, a pigment first discovered in 1804 by the French chemist Thenard.

Figures 1–6 are photomicrographs of cross-sections serving to illustrate the varied appearance to be observed in the build-up of paintings of different periods by different artists. In figure 1 the layers 1–4 represent the original painting, which dates from 1530 to 1535; the ground is chalk, and the red layer consists of an iron oxide pigment upon which paint layers containing blue azurite and green malachite are superimposed. The subsequent layers consist of dark overpaints in oil and varnish which were applied about 1740. The sharp division between the original and the overpaint is clearly marked: incidentally, the painting has been now restored to its original condition by the removal of the eighteenth-century overpaint. Figure 2 is typical of the technique of early Flemish paintings, comprising compact, relatively thin and regular paint layers. Figure 3 is of interest because it shows how original paint-losses have been covered by repainting. The light blue layer 4 consists of azurite in a pure oil medium; it represents the original Holbein paint. At some time, fragments of this flaked off, uncovering the white underpaint (layer 3), and the resulting lacunae were overpainted. Thus layer 5 (which is rather greener than it appears in the reproduction) consists of a mixture of azurite and white lead in an oleoresinous medium. This would turn a dirty olive-green as the medium yellowed, and probably explains why a repaint containing Prussian blue (layer 6) was applied at a later date. Figure 4 is characteristic of the technique employed by Rembrandt in his later period, being similar in its general features to other late paintings by this artist. The paint, rich in oil, is laid on in relatively thick layers. The ground shown in figure 5 has the coarse crystalline structure typical of that used by many Venetian painters.

CHROMATOGRAPHY OF NATURAL RESINS

The chemical examination of paint-media and varnishes, especially as regards the detection of natural resins, presents a more difficult problem than the identification of pigments, for which precise sensitive tests are available. This is due to the chemical complexity of the materials involved.

The natural resins, properly so called, are hydrophobic substances of terpene-like character, and are to be distinguished from the gums, which consist largely of water-soluble polysaccharides. However, there are also intermediate substances, such as asafoetida, myrrh, and frankincense, which

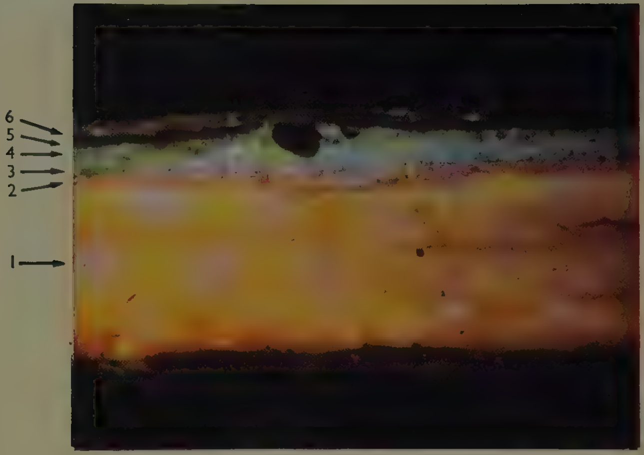

FIGURE 1 – *Fragment of discoloured green paint from a panel-painting in Chichester cathedral. Layers 1–4 represent the original paint. Above them are layers of later overpaints in oil and varnish.* (× 95)

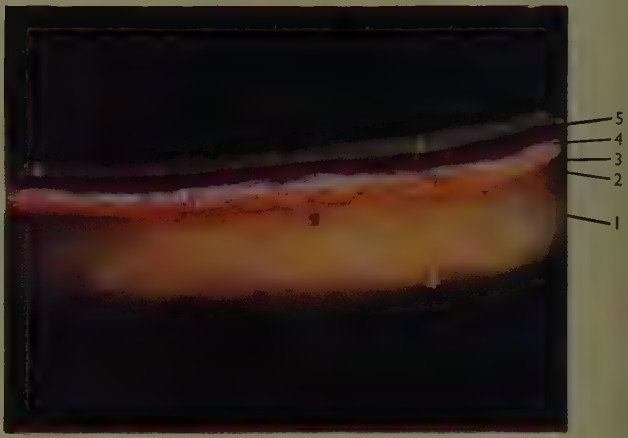

FIGURE 2 – *Paint-fragment from picture on the back of a panel-painting by Gerard David* (1450 *or* 1460?–1523). *Layer* 5 *is a dirty grey paint covering the picture. The reddish paint in layers* 2–4 *consists of iron oxide pigments of different shades mixed with white lead.* (× 95)

FIGURE 3 – *Fragment of blue paint taken from the background of a Holbein* (1497?–1543) *painting. This cross-section shows the complete system of layers from the wood of the support* (*layer* 1) *to the varnish* (*layer* 7). (× 95)

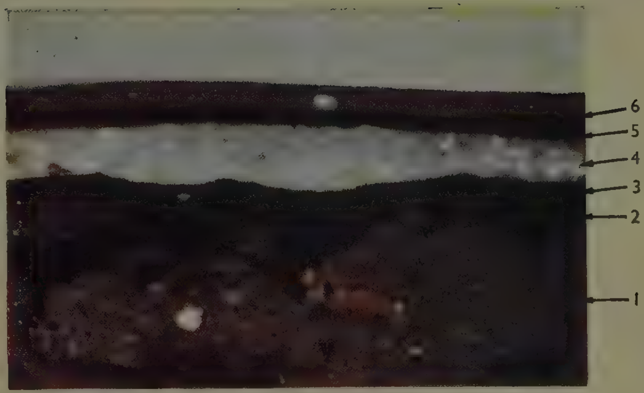

FIGURE 4 – *Paint-fragment from the area of a shadow on a hand from a late Rembrandt (1606–69) portrait. Note the use of a dark ground (layer 1) used to prime the canvas support; also the coarsely-ground white lead in layer 4.* (× 95)

FIGURE 5 – *Fragment of ground from painting by Giovanni Bellini (1430?–1516). The thick ground has been built up in a series of separate layers. The dark brown colour is due to the presence of an unusually high proportion of glue.* (× 95)

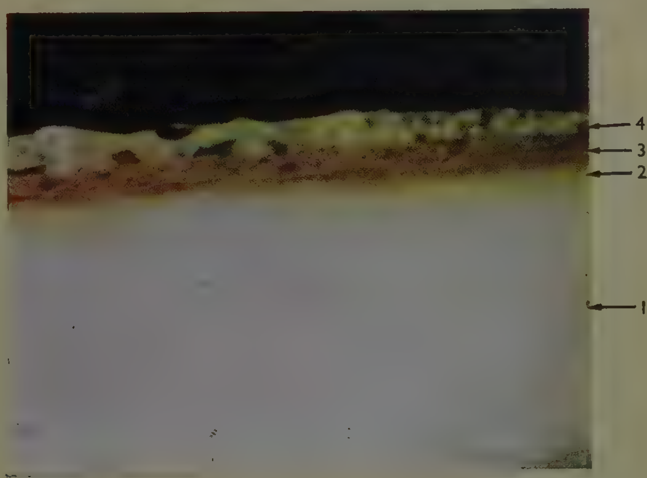

FIGURE 6 – *Fragment of brownish-green paint representing foliage, from a painting by Pollaiuolo (1429–98). Note in layer 4 the large transparent dark green crystalline particles of verdigris, which are embedded in a matrix of white lead coloured with copper resinate. On the surface the latter has turned brown.* (× 95)

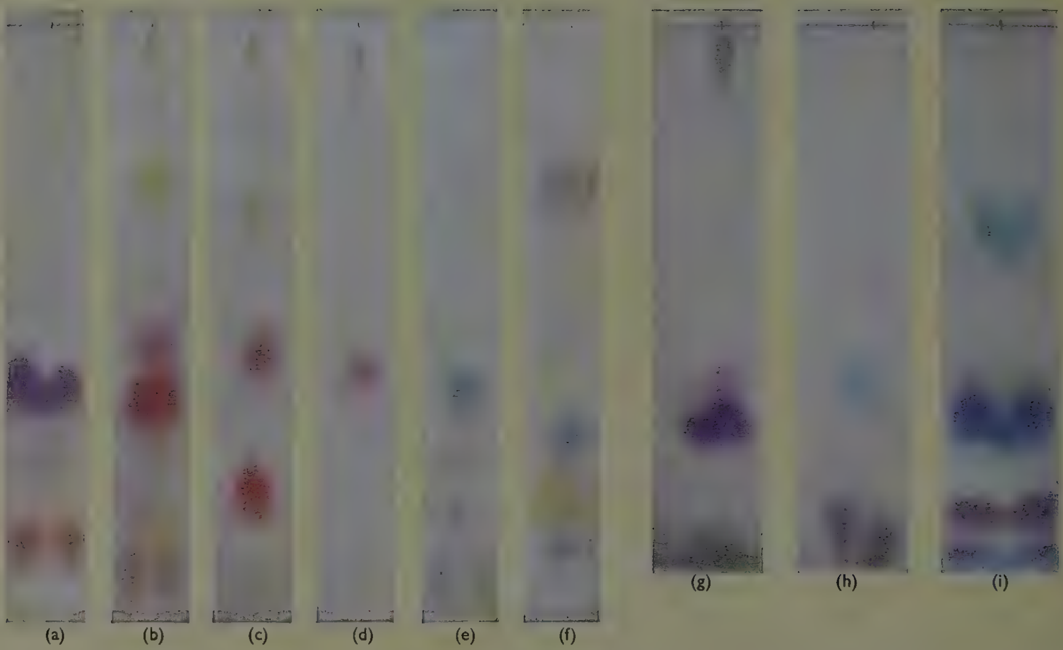

FIGURE 7 – *Reverse-phase partition chromatograms, on filter-paper, of some natural resins.* 0·1 *mg of the resin in a volatile solvent is placed at the top of the strip of filter-paper impregnated with the stationary phase (odourless kerosene). The mobile phase used for elution consists of iso-propanol* (65 *parts) and water* (35 *parts).*

(a) *Rosin. This consists largely of abietic acid, which is responsible for the main blue spot.*

(b) *Mastic. From* Pistacia lentiscus.

(c) *Dammar. From various species of* Hopea. *The five spots visible are (reading downwards): β-resene, triterpene monoketones, monohydric alcohols, keto-alcohols, and a mixture of diols and a keto acid.*

(d) *Congo copal. Fossil resin said to originate from* Copaifera demeusei. *Only the chloroform-soluble portion of the resin has been used in preparing this chromatogram.*

(e) *Copaiba. Balsam from* Copaifera langsdorfii *and similar species.*

(f) *Manila elemi. From* Canarium luzonicum. *The zone at the top is due to a mixture of α- and β-amyrin.*

(g) *Canada balsam. From* Abies balsamea. *The main blue spot is probably due to abietic acid. (Strasbourg turpentine from* Abies pectinata *gives an identical chromatogram.)*

(h) *Sandarac. From* Tetraclinus articulata.

(i) *Venice turpentine. From* Larix decidua. *Once again the main blue spot is probably due to abietic acid.*

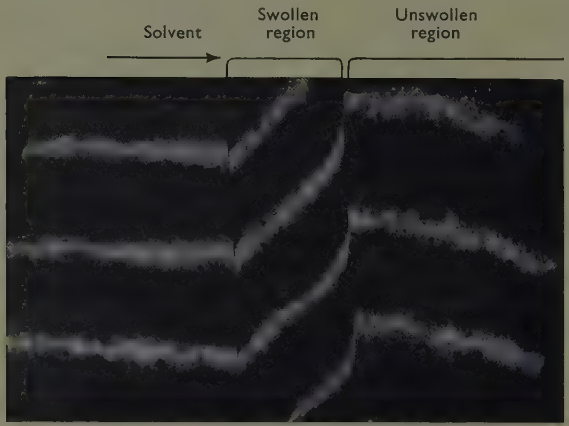

FIGURE 8 – *Swelling of oil varnish in xylene.*

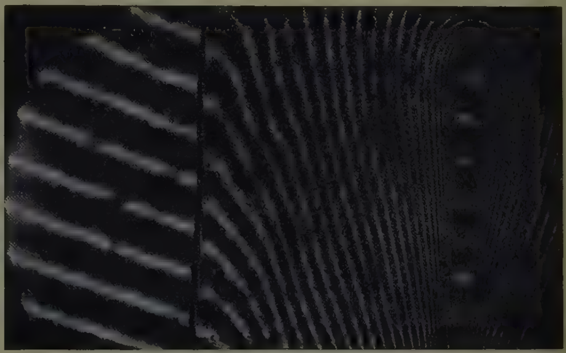

FIGURE 9 – *Swelling of oil varnish by acetone.*

consist of a mixture of materials belonging to both these classes; they are known as oleo-gum-resins. The natural resins themselves are rather arbitrarily subdivided into the solid, typical varnish resins, which include dammar, mastic, copals, and rosin, and the oleo-resins or balsams, such as the turpentines, copaiba, and elemi. The latter contain a higher proportion of essential oil and are syrupy or semi-solid at ordinary temperatures. The difference between resins and balsams is one of degree only; evaporation of the excess of essential oil in a balsam will leave a solid resin. Thus the oleoresin turpentine from Coniferae yields rosin when the essential oil is distilled off.

Although natural resins have been the subject of extensive chemical investigation for about 150 years, the early results achieved, which are very fully reviewed by Tschirch and Stock [4], leave one with a picture of intimidating complexity and some doubt as to the homogeneity of many of the compounds described. This is due largely to the fact that the methods then available for the isolation and purification of the majority of the resin components were not adequate. The early work was devoted largely to the acidic constituents and, despite the fact that the two crystalline triterpene alcohols α- and β-amyrin were isolated from elemi over fifty years ago [5], comparatively little work has been done on the analysis of the neutral fractions of natural resins. There has been a tendency to group them together under the vague names of α- and β-resenes. Our present work on the chemistry of dammar and mastic suggests that, for these resins and no doubt for others also, the distinction between the alcohol-soluble α-resene and the alcohol-insoluble β-resene has a sound basis. It has, however, been found that the α-resene fraction is a complex mixture of triterpene alcohols, ketones, ketols, and the like, whereas the β-resene fraction consists of a mixture of polymeric materials of low oxygen-content having a wide range of molecular weights.

The primary stimulus to apply reversed-phase paper chromatography to the examination of the constituents of natural resins lay in the need for devising a trustworthy method of identifying these resins when present in paint-media. It was found that fresh natural resins could in fact be readily distinguished chromatographically using a reversed-phase system specially elaborated for this purpose [6]. However, the original problem still remained largely unsolved, since it was found that, even after a few years, natural resins in thin films are completely oxidized and no longer give distinguishable chromatograms using this system. Instead, these show a single spot of high R_f value, corresponding to the polar oxidation products. At the very least, such a spot points to the presence of a natural resin in a paint medium. The problem has therefore now assumed a different form, namely the development of a suitable method of analysing these oxidation products.

As in other fields, paper chromatography will probably be of most use as a convenient method of following the course of the isolation of di- and triterpene constituents from resins and other natural sources. Moreover the technique provides a certain amount of information about the nature of the constituents themselves, since their positions in the chromatogram are dependent primarily upon the number and nature of the functional groups present. In a reversed-phase system such as this, the more polar the constituent the farther it travels from the origin.

In figure 7 are reproduced paper chromatograms of selected resins. In them, the positions of the resin constituents have been located using the Halphen-Hicks reaction [7]; the chromatogram is sprayed with a solution of phenol in carbon tetrachloride and then suspended in bromine vapour for a short time.

DIFFUSION PHENOMENA IN FILMS

One of the recurrent problems of conservation concerns the action of solvents on varnish and paint. Before any picture can be cleaned, the twin questions of what solvents to apply, and in what strength, must be decided, and in the absence of any basic knowledge these decisions can be made only in the light of custom, experience, and trial-and-error. The nature of the problem is complex, the factors are many, and the complete answer is still a long way off. Of the many aspects that must some day be examined, three have been chosen for preliminary work: the process of diffusion of solvents into varnish, the solvent power of mixed liquids, and the mechanical properties of swollen varnishes.

There is a particular interest in the mechanism of swelling, because whereas the spirit-varnishes composed wholly of soluble resins are easily removed, the really troublesome cases are always those in which the resin has been mixed with a drying oil. Such a varnish may be almost entirely insoluble in organic liquids, and will merely swell and become to a certain extent softer, thus allowing of its removal by gentle mechanical action.

The diffusion of solvents through cellulose

acetate and other polymers has been studied by Robinson [8], and although the polymers he used have few similarities to oil varnishes, his technique of interference microscopy is appropriate. A film of varnish is clamped between half-rhodiumized glass plates arranged at a small wedge-angle, and is examined by monochromatic light collimated to a parallel, normally incident beam. As the solvent —or, more accurately, penetrant liquid—advances into the material from the edges, the change in refractive index causes a distortion of the Fizeau fringes, from which the gradient of concentration can be calculated. The boundary between swollen and unswollen material has in every case appeared sharp: the typical sudden change in refractive index visible in figure 8 points to a process of solvation of the linoxyn structure, while the ensuing gradual change in refractive index through the swollen material is due to true diffusion. Figure 9 shows a late stage in a diffusion experiment. The varnish is fully swollen near the edge, the small slope of the fringes showing that the gradient of concentration is low there, and only a narrow island of unswollen material remains. A complete analysis of the fringe pattern is made difficult by the leaching-out of soluble resins and unpolymerized oil. Still, the technique is capable of yielding a qualitative description of events in simulated cleaning operations: for example, one can see how far the varnish is penetrated when flooded with a penetrant liquid for a limited time, then with a non-penetrant, miscible with the first and tending to withdraw it from the varnish.

Mixtures of organic liquids are invariably employed by restorers, who have come to recognize, broadly speaking, two classes of liquid: penetrant liquids or solvents, and non-penetrant liquids or restrainers, typified by ethyl alcohol and white spirit respectively. Our experiments show that, in fact, mixtures of these may have a swelling-power much greater than either used alone; thus a 60 : 40 mixture of turpentine and ethyl alcohol will eventually swell a linoxyn film to three times the extent caused by alcohol alone. This large equilibrium-swelling is, however, only slowly reached, and in practice turpentine can be regarded as a restrainer for ethyl alcohol, slowing down its initial action.

In its mechanical properties linoxyn has been found to have certain resemblances to rubber, becoming as it were slowly more vulcanized with age and exposure to light. From the point of view of conservation it is important to find out the influence of age, humidity, and swelling by solvents on these mechanical properties, but the measurement of any single elastic constant is not a simple matter. Recent advances in rubber technology should help in suggesting experimental methods and in interpreting the results.

An example of this work may be quoted. The brittleness of samples of varnish, varying inevitably in thickness, is measured, not with reference to the smallest mandrel over which they may be bent without cracking, but as the highest temperature at which a sample ruptures during a 20 per cent extension at a standard rate. In this way one can measure the increase in brittleness due to the removal of unpolymerized oil by solvents, or the decrease that can be brought about by the introduction of plasticizers. Such plasticizers can be added to dried-up and brittle films if applied in admixture with a liquid of good swelling-power. The function of the latter is to expand the cross-linked linoxyn structure, which acts as a molecular sieve, and so to permit the entrance of bulkier molecules; afterwards the volatile liquid is allowed to diffuse out and evaporate, leaving the plasticizer locked within. A rather brittle specimen of oil varnish was left in dinonyl adipate for five months, during which time a small quantity was absorbed—enough to change by 5° C the temperature at which fracture occurred in the test for brittleness. The same change could be induced in 18 hours by soaking the specimen of varnish in a 4 : 1 mixture of dinonyl adipate and benzene; in this case the brittleness was not measured until a month had passed, to ensure the complete removal of benzene. These and other experiments on the swelling of varnishes are more fully described in a paper read at the conference of the Oil and Colour Chemists' Association last year [9].

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Biochemical light upon an ancient poison: a lethal synthesis

SIR RUDOLPH PETERS

A decade ago, the toxic principle of the South African plant *Dichapetalum cymosum* was shown to be fluoroacetic acid. Subsequent study of this substance has led to biochemical discoveries of great interest. The action of fluoroacetate, itself innocuous, proves to be due to its conversion by enzymes into a toxic substance; this is precisely the opposite of the detoxication mechanism by which the body commonly attempts to eliminate poisonous substances.

For a long time it was thought that once a chemical substance entered the protoplasm of the cell it ceased to behave as such, but this view is now entirely obsolete. Differences may indeed appear in the behaviour *in vivo* as distinct from that *in vitro*, but the explanation for these is sought in the organization of the tissue. Thus the advances made in the last twenty years in our knowledge of the details of the disposal in the higher animals of pyruvic acid have taught us the dependence of this stage in metabolism upon some members of the vitamin B complex, namely thiamine, nicotinic acid, and pantothenic acid. They have also shown that a complicated system of enzymes is required in the conversion of the acid to carbon dioxide and water, involving a synthesis of C_2 fragments to form a C_6 tricarboxylic acid as an intermediate stage. Since pyruvic acid is a half-way stage in the degradation of sugar, it is not surprising that failure in the metabolism of pyruvate is attended by dire consequences in the brain, which is mainly dependent for its normal functioning upon the energy derived from the glucose brought to it in the blood stream. Though much remains to be done, knowledge has now advanced enough to enable us to make a limited analysis of the biochemical lesion in some toxic states; by this is meant the first deviation from normality in the tissue. In this short review it is proposed to show how the existence of a lethal synthesis has been unravelled in connection with the toxic action of a plant poison.

The substance fluoroacetic acid, $F.CH_2.COOH$, has a remarkable historical background; it was first known in chemistry from the synthesis by Swarts at Ghent in 1896 [1]. For over forty-five years no one suspected that it was also a natural product, but in 1943 Marais [2] found that it was the toxic principle of the South African poisonous plant *Dichapetalum cymosum*, known locally as *Gifblaar* (figure 1); in other words nature had carried out its synthesis long before man. Marais' brilliant isolation was the culmination of several earlier attempts [3].

Dichapetalum cymosum is largely confined to the Pretoria region of South Africa, and the plant flourishes there on particular slopes; twice a year the fresh leaves are so poisonous that 20 g are sufficient to kill a sheep. The poison is water-soluble. Eradication of the plant is difficult owing to the extensive, branching, underground-stem system; it is apt to grow among rocks, and it has been necessary to erect fencing to keep cattle from the weed [4]. It is clearly of agricultural importance to try to obtain an antidote. As the action of the fluorine compound is very subtle, it became necessary to conduct a deep biochemical analysis of this action, which will be considered here before its application to the pharmacology.

It so happened that in 1941 some observations were made on both sides of the Atlantic upon the action of this poison upon enzymes, as a purely defensive measure. These revealed the curious fact that, unlike arsenicals, iodoacetate and some other poisons, fluoroacetate had no action upon isolated enzymes. Its toxicity cannot be due to the liberation of fluoride ion because of the extreme stability of the CF bond, withstanding as it does the action of hot concentrated sulphuric acid [5], and there is no evidence as yet of any enzyme in the higher animals that can break this bond. Further knowledge of the action of this toxic agent was imperative (*a*) if the hope were to be fulfilled of getting an antidote for the poisoned cattle, (*b*) because it formed a marked exception to the rule that poisons attack enzymes, and (*c*) because of its probable scientific and medical interest.

When the writer returned to the study of this

poison with C. Liébecq in 1947, two significant facts were available [6]. First, from an extensive research with varied synthetic organic compounds containing the CF bond, B. C. Saunders and his colleagues [7] had concluded that the active entity was FCH_2CO—; for instance, straight chain compounds containing 2, 4, 6, 8 C atoms were toxic, whereas 3, 5, 7 C and so on were relatively non-toxic. It was somewhat like the well known Knoop rule for the fatty acids. Secondly, Bartlett and Guzman Barron [8], though they could not find any effect upon isolated enzymes, had noticed an accumulation of acetate in poisoned slices of tissue, from which they concluded that the fluoroacetate inhibited acetate oxidation competitively. We soon found, in poisoned particle-preparations from kidney, conditions in which there was a lowering of oxygen uptake with no change in acetate concentration; the enzyme preparations were reinforced, as is customary in this type of work, with adenosine triphosphate and magnesium, and were given fumarate as the substrate.

FIGURE 1 – Dichapetalum cymosum (*Gifblaar*), *showing the underground stem system.* (*From Burt Davy.*) (Proc. Roy. Soc. B., **139**, 143, 1952.)

It was clear, therefore, that Bartlett and Barron's hypothesis was not the whole story. Further search brought to light the fact that an accumulation of citrate accompanied the decrease in oxygen uptake. We were thus led to advance the hypothesis in 1948 [6] that the fluoroacetate behaved somewhat like acetate in metabolism, that it was transformed by the reactions of the tricarboxylic acid cycle to form a fluorotricarboxylic acid, which then jammed oxidation of citrate. Figure 2 illustrates very diagrammatically the final course of the oxidation of the C_2 fragments derived from pyruvate, and figure 3 the 'jamming' hypothesis. A similar view was put forward independently a little later by Martius [9]. The idea that the citrate accumulations were an important factor of the poisoning was considerably strengthened when it was found by P. Buffa and the writer [10] that

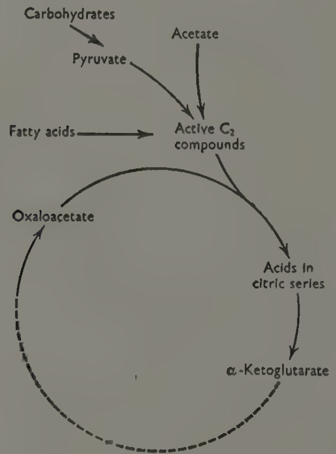


FIGURE 2 – *Diagram of main stages in tricarboxylic acid cycle (see Krebs, 'Advances in Enzymology,' Vol. 3, 1943). Pyruvate, after decarboxylation and activation to a C_2 fragment (now known to be acetyl-coenzyme A (Lipmann)), condenses with the C_4 acid, oxaloacetic acid, to form the C_6 acid, citric acid. By degradation to a C_5 acid and then to C_4 acids, oxaloacetic acid is again regenerated. During the degradation CO_2 and H_2O are eliminated, thereby completing oxidation of the C_2 fragment. The biological reason for these complications is unknown.*

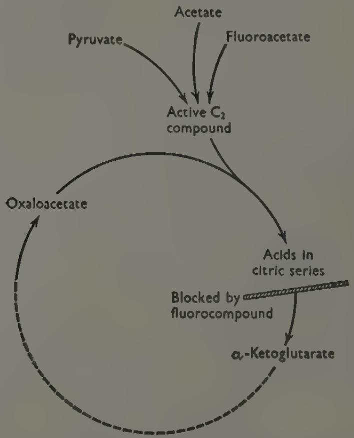
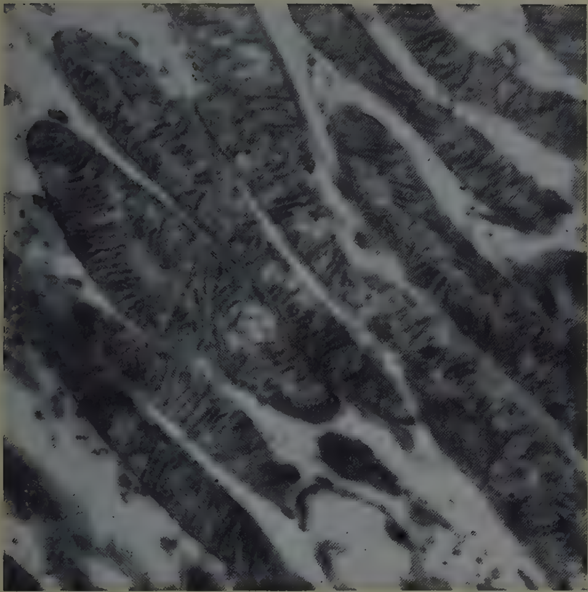


FIGURE 3 – *'Jamming theory.' After activation to a C_2 fragment fluoroacetate is condensed to form fluorocitric acid, which then 'jams' further degradation of citric acid.*



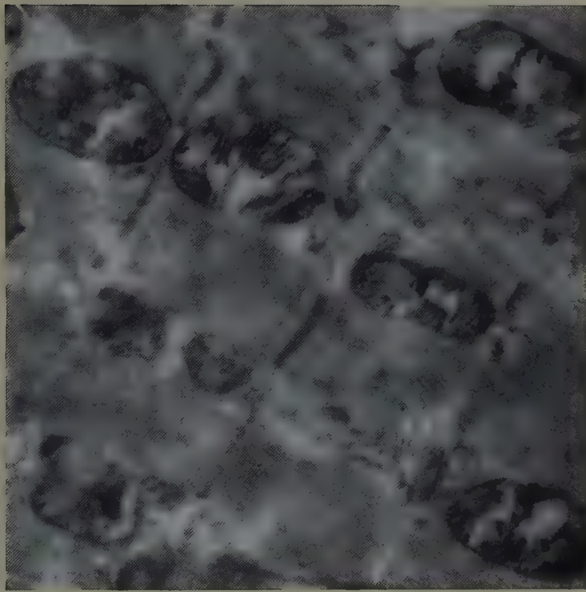


FIGURE 4 – *Electron micrographs of mitochondria (J. Histochemistry and Cytochemistry,* 1953, 1, 188)*; section cut by the microtome described by A. Claude, Harvey Lectures,* 1948, *XLIII, p.* 152*; approximate thickness less than* 0·05 μ. *The tissues were fixed in buffered osmium tetroxide at* p*H* 7·3 *and embedded in polymerized methyl methacrylate. Left: rat kidney mitochondria* (× 22 850). *Note the fine structure, especially the internal ridges* (cristae mitochondriales) *protruding towards the interior of the organelles. There is a membrane present about* 7 *m*μ (70 *A*) *thick. Right: rat myocardium* (× 22 500). (*Photographs by G. E. Palade, Rockefeller Institute.*)

FIGURE 5 – *Beginning of a fit due to the intracranial injection (under ether anaesthesia) of fluorocitrate.* (Brit. med. Bull., **9**, 116, 1953.)

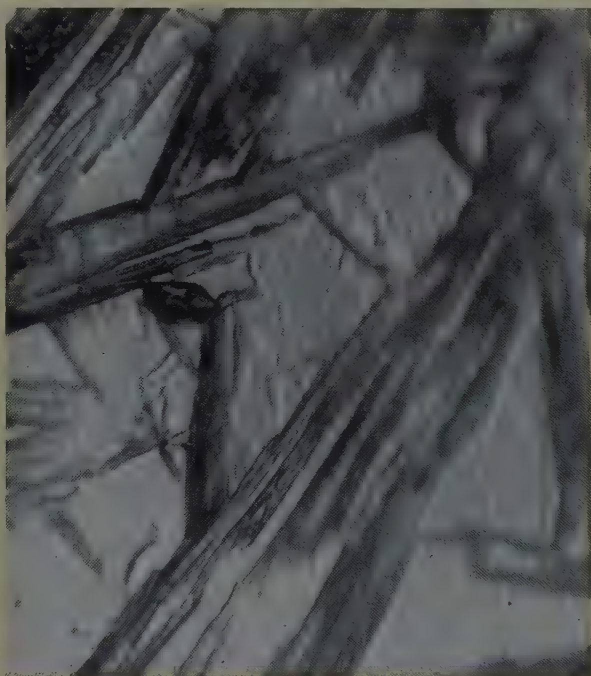


FIGURE 6 – *Crystalline specimen of fluorocitric acid.* (Proc. Roy. Soc. B., **140**, 497, 1953.)

FIGURE 7 – Dichapetalum toxicarium (*p.* 153). *Photographs of dry drupe (the nut-like fruit containing the seeds) and of the separated seeds. (Natural size.)*

fluoroacetate poisoning *in vivo* leads within the short time of 30–60 minutes to remarkable accumulations of citric acid in various organs: in kidney this may be 80 times the normal, in heart 20 times, in brain 8 times. The effects are evidently general; they have been demonstrated in the rat, mouse, rabbit, guinea-pig, dog, and pigeon. The fact that there are no increases in the concentration of pyruvate or of α-ketoglutarate limits the action definitely to the tricarboxylic acid stage of the cycle. It was clear that progress could be made only by isolation of the fluoro-compound, if it existed, especially since by this time others had found the increase in citric acid *in vitro* and were suggesting that it was due to an increased formation rather than a decreased oxidation [11]. When we embarked upon it, we little realized that it would take us four years to prove that the compound synthesized enzymically was actually the new compound monofluorocitric acid:

$$HOOC.CHF.\mathbf{C}(OH)(COOH).CH_2.COOH.$$

Some remarks upon the details of the isolation will indicate the special difficulties encountered. The best way to make the inhibitor was to synthesize it with kidney particles in a phosphate-potassium chloride medium from fumarate and fluoroacetate. Attempts to do this on a really large scale with ox kidney failed, so that the tissue used came mainly from the guinea-pig and rabbit, and occasionally from the kidneys of dogs. Preparations were tested by using centrifuged kidney particles (from guinea-pigs); the capacity of a supposed fluorocitrate fraction in stopping the removal of citric acid in 30 minutes at 38° C formed a basis of comparison for isolation. The kidneys of one rabbit made about 1 mg of fluorocitrate; this had to be separated from much larger amounts of citrate and phosphate. We were much misled for months by failure to realize how little fluoro-compound was causing the inhibition. Eventually, by finding, first, that the required inhibitor was more acidic than phosphoric and citric acids and that, therefore, it would be precipitated at a lower *p*H with lead salts, and, secondly, that it required a stronger acid to remove it from a column of amberlite resin (IRA 400) than citric or the last traces of phosphoric acid, fluorocitric acid was separated in small amounts (7 mg) as a crystalline and very hygroscopic compound (figure 6) [12, 13].

The presence of a CF compound was demonstrated by infra-red spectrometry, and the fluorine content was estimated spectrochemically in the special bands for F, viz. 7128 A and 7200 A respectively [14]. The latter method is new and very powerful; it not only makes the presence of fluorine certain, but is capable of estimating as little as a few μg of it. The final proof that the compound was a citrate (rather than an isocitrate) depended upon a synthesis of fluorocitric acid by Rivett and comparison of the spectra [15].

The fluorocitric acid synthesized by the enzymes is a very potent inhibitor of citric acid metabolism in the kidney particles: to make this precise, the effect of less than 1 μg can be determined in the presence of 1·92 mg (10 μmol) of citric acid. It can be seen from the formula that there should be four stereoisomers present in the synthetic specimens. From this it might be inferred that the synthetic compound would be less active than the natural; experiments show that it has about 50 per cent of the activity, suggesting that only one of the optically active **C** atoms matters for the inhibitory activity.

Our next inquiry must be whether there is proof that the enzymes concerned with the tricarboxylic acid stages of the cycle are inhibited. It will be seen from figure 8 that only two enzymes are likely to be concerned, aconitase and isocitric dehydrogenase. The latter carries out the change of the C_6 compound, isocitric acid, to the C_5 compound α-ketoglutaric acid, and is not affected by fluorocitric acid [12]. This reduces the problem to that of the behaviour of aconitase. This remarkable enzyme is a most appropriate tool for this stage in metabolism because, by its action in altering the position of the OH group, it prepares the way for the subsequent decarboxylation of the α-keto compound. Until recently, the instability of this enzyme has been a difficulty in research, but taking advantage of the findings in Sweden that citric acid can stabilize it, and in the U.S.A. that ferrous iron and cysteine are needed for full activity [16], it has recently been tamed in the writer's laboratory [17]: purified preparations will remain stable for months in the cold. With this isolated and soluble enzyme it has now been established that the natural fluorocitric acid is a competitive inhibitor [18], thus bearing out preliminary indications [19]. This can account for the observed inhibition; but, as often happens in research, certain subsidiary facts have appeared that are not yet properly understood.

The particle-preparations from kidney that have been used for the inhibitor tests are 10–20 times more sensitive to the effect of the fluorocitric acid than is the soluble aconitase enzyme. This leads one to ask what are the differences of constitution of these particles; recent research (started by Bensley and continued by Claude, Hogeboom, Schneider, and others) has elucidated the fact that the preparations of particles obtained in this way are in fact preparations of the mitochondria from the insides of the tissue cells. These mitochondria (perhaps 2 μ long and 0·5 μ wide) are evidently the seat of activity of the enzymes oxidizing pyruvate, which include the enzymes of the tricarboxylic acid cycle. Indeed, there have been experiments done recently in the Rockefeller Foundation in which photographs with the electron microscope show a somewhat highly organized structure in the mitochondria (figure 4). In the cell, therefore, the enzymes concerned are, as it were, shut up in these mitochondrial bags. We are dealing, in particle preparations from kidney, with these bags of enzymes, probably structurally organized; at any rate they have a permeability barrier which separates them from the medium in which they are suspended. Somehow these factors are sufficient to magnify the effects observed when fluorocitrate acts upon the aconitase enzyme inside the mitochondrion. How and why these differences occur is still unknown, but a matter of far-reaching significance is probably raised.

The next question to be considered is whether in fact the compound fluorocitrate can be responsible for the lethal effect of fluoroacetate. Some remarks are necessary about the poisoning signs seen with fluoroacetate. The doses required to kill different animals vary very much. The dog is killed by 0·06 mg/kg, whereas the toad will stand doses of 500 mg/kg. In the intermediate range, we

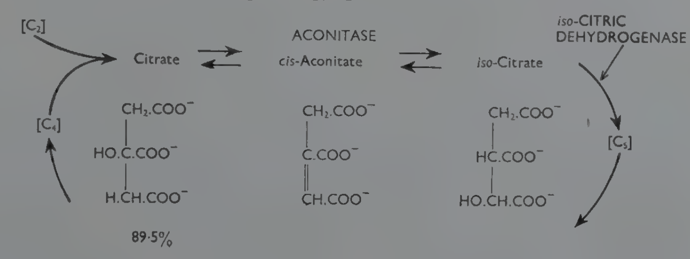


FIGURE 8 – *The reactions of the tricarboxylic acid cycle effected by the enzymes aconitase and isocitric dehydrogenase.* (Proc. Roy. Soc. B., **139**, 143, 1952.)

have the doses for various other animals [20]; for instance, the rabbit will be poisoned by something like 0·2 mg/kg, whereas the rat will require a dose of 5 mg/kg. These strange differences can probably be correlated with different powers of activating acetate, though this matter still awaits a proper proof. The monkey requires a somewhat larger dose, upwards of 15 mg/kg. It seems that man also is relatively insensitive; this was proved by E. D. Adrian, who took a dose sufficient to produce a urine toxic to guinea-pigs. There are two classes of signs found in varying degree in different animals. Some, like the dog, show signs chiefly in the nervous system; others, like the rabbit, are mainly affected in the heart, getting (for example) fibrillation. The rat shows both signs in varying degree. After lethal doses there is usually a period of delay of about 20–25 minutes. The animal then appears to be worried and shortly afterwards may go into a rigid tetanic convulsion.

It has been possible recently to prove that the fluorocitrate is itself the toxic agent by injecting it, under ether, within the skull of the pigeon. After an injection of some 30 µg of enzymically prepared fluorocitrate, the animal comes round from the anaesthetic and is normal for a short period of ten minutes or so; it then becomes agitated and finally enters upon convulsions having some resemblance to those produced by thiamine deficiency, though usually there is more wing movement to be seen (figure 5). The fits kill the animal quickly. As little as 11 µg of fluoro*citrate* has sufficed to throw an animal into such a condition. On the other hand, an intracranial injection of fluoro*acetate* in larger amounts gives no convulsions at all. This fact is consistent with the indirect evidence that brain tissue does not synthesize fluoro*citrate* from fluoro*acetate*, and suggests that convulsions occurring after intraperitoneal injections of fluoro*acetate* are due to penetration to the brain by fluoro*citrate* synthesized elsewhere. Since these fits can be induced by fluorocitrate, it is, in the writer's opinion, definitely proved that in fluoroacetate poisoning there is a lethal synthesis brought about by the action of the body's own tissue enzymes.

The research has demonstrated two things fairly clearly. First, the citric acid cycle must be a reality *in vivo*. Secondly, though this appeared to be an exception to the general proposition that toxic substances poisoned intracellular enzymes, now it is seen to fall into the general rule. Several other questions are left that are worth discussion. First, what is the mechanism by which these convulsions are produced, and is there any chance of reversing them? [21]. Secondly, supposing we are unsuccessful in reversing them, can we protect the animals by stopping the synthesis of fluorocitrate in some way, and so avert the toxicity? Thirdly, arising out of this, is there any other possible medical application? Finally, when all these points are settled, a further question arises, namely whether there are any other examples of this type of lethal synthesis.

These questions will be dealt with in order. In considering what causes convulsions, two thoughts immediately occur; the first is that stopping pyruvate oxidation at the stage of citric acid must cut off the energy supply to a large extent. In other examples of interference with pyruvate oxidation in the pigeon brain, rather similar signs appear, e.g. in thiamine deficiency and arsenical intoxication; further, a reduction of sugar in the blood by cutting off the sugar supply with insulin also leads to convulsions. In all these cases there is an interruption of the energy supply sufficient to throw some parts of the brain out of order, so causing the dysfunction which is reflected in the signs observed. In the case of the fluorocitrate-induced fit there is, secondarily, a further possible factor of complication. The increasing amount of citrate might be expected, quite reasonably, to interfere by combination with any calcium concentration in the tissue. It has been well known for many

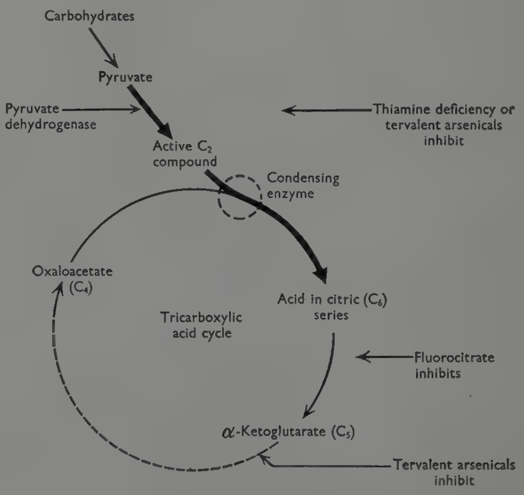


FIGURE 9 – *Diagrammatic representation of the course of oxidation of pyruvate by the pyruvate oxidase system, showing the stages at which vitamin B_1 (thiamine) deficiency, tervalent arsenicals, and fluorocitrate respectively stop the oxidation. Each of them can induce fits.* (Brit. med. Bull., **9**, 116. 1953.)

years that interference with the calcium concentration which bathes the nerves will induce a hyper-excitable state; for instance, Hastings and colleagues [22] have shown that a decrease in the concentration of calcium in the cerebro-spinal fluid is enough to cause convulsions in dogs, and these convulsions may be stopped at once if the calcium bound by the injected citrate is replaced. There is a difference in the site of citric acid accumulation in fluorocitrate poisoning, because this accumulation occurs inside the cells and not in the medium that is bathing them. One authority considers that the amounts of Ca^{++}, if any, inside cells are negligible [23]. Some extensive experiments with pigeons and also with rabbits have led to the conclusion that it is impossible to reverse these fits by injection of calcium [24]. As yet, therefore, there is no experimental evidence that they are due to interference with the balance of inorganic ions. This whole question is still *sub judice*. It has been found that there is no direct correlation between the citric acid accumulation and the convulsive state. This would not be expected on physiological principles. It has also been shown that in one animal at least, namely the horned toad, large accumulations of citrate can occur in the heart without apparent disturbance of function [25], facts which are difficult to interpret. They might merely mean that the calcium injected into the cerebro-spinal fluid does not penetrate the barrier and get at the site which is poisoned by fluorocitrate. What can be definitely stated is that the action of the fluorocitrate upon aconitase induces the biochemical lesion which starts the neurones concerned upon the path leading to hyper-excitability.

With regard to the chances of reversing these signs, and so curing the animal, which was one of the purposes of the research, neither we nor others have had any success with injection of members of the tricarboxylic acid cycle. It might well have been expected that some of these acids might cure by displacing the fluorocitrate. It is not known whether this failure is due to the difficulty of penetration to the active site; but at the moment this line of approach has failed, and recourse has had to be made to protection rather than to reversal of the condition once it has become established. After the early work done with acetate, various attempts were made to reduce the severity of the conditions, either with acetate or by injection of C_2 substances such as alcohol. These substances have had only a limited success except in one case: Chenoweth and his colleagues [26] found that glycerol monoacetin would avert death when injected shortly after a lethal dose of fluoroacetate. This they believe to be due to the presence inside the cell of the C_2 fragment introduced by the glycerol carrier. A somewhat similar explanation has been given by Gitter, Blank, and Bergmann [27], who used acetamide for protection with similar success.

These results suggested that it should be possible to fill the logical gap in the biochemistry by showing that C_2 substances stop the formation of fluorocitrate from fluoroacetate *in vitro*, and this has been done in our laboratory: small amounts of acetate will stop the synthesis *in vitro* from relatively larger amounts of fluoroacetate.

POSSIBLE MEDICAL AND SCIENTIFIC APPLICATIONS

The possible medical and scientific applications of the facts described centre round interference with the metabolism of pyruvate in general, and at the aconitase stage in particular, with its indicator of increased citrate concentration (figure 9). It may be noted that the increase in citric acid induced may be expected to have forensic application in providing non-symptomatic evidence in confirmation of suspected fluoroacetate poisoning. Beyond thiamine deficiency and arsenical poisoning, the only other instance known at present of an agent which produces interference with pyruvate oxidation coupled with objective medical signs is that of the alkaloid sanguinarine, associated with the seeds of *Argemone mexicana* and a contaminant of mustard oil [28]; there is a strong possibility that this may be responsible for epidemic dropsy. Regarding interference at the citric acid stage, we still know little, but it is probable that a search would produce clinical applications.

In the fluorine field, some progress has been made in the writer's laboratory [21] towards the isolation of the active principles from another species, *Dichapetalum toxicarium*, also called ratsbane; this plant, found in the Sierra Leone district, has been used by witch-doctors, and produces the condition known as 'broke back,' strongly resembling a neuronitis (figure 7). We have proved that injection of extracts of the seeds induces citric acid accumulation *in vivo*, and small amounts of fluorocitrate have been isolated, indicating the close connection with the observations made upon the active principle of *Dichapetalum cymosum*. In this instance a direct medical application is in sight in the sense of an understanding of the underlying biochemical causation of 'broke back.'

CLOSING REMARKS

To sum up, though the deep biochemical analysis briefly described has indicated what must be done to reverse the poisoning, it has also shown clearly that this is made specially difficult by the necessity of penetrating into the mitochondrion without disturbing its organization. Nevertheless, the protective effect of C_2-containing substances can now be logically explained as due to interference with the synthesis of fluorocitrate. This research leaves little doubt of the reality of the citric acid stage of the tricarboxylic acid cycle *in vivo*, which the work of Krebs and others has done so much to establish *in vitro*. There is now a new agent for inhibiting the cycle reactions *in vitro*, as well as a selective inhibitor for aconitase. There is also now available another convulsive agent inducing a biochemical lesion which is understood in principle and which should therefore prove a useful tool in studying the initiation and cause of some fits. Again, one instance has been thrown into relief in which a 'mitochondrial' enzyme behaves differently from the same enzyme in solution; this may prove of far-reaching importance. It is the writer's opinion that the above dividends have come from conducting this type of biochemical analysis; it was used in the arsenical and British anti-lewisite researches and, though it is slow, the writer believes it to be the best hope of advancing the cause of logical therapy.

The lethal synthesis revealed and proved here for the first time has to be distinguished from toxic conversions such as occur with arsenical drugs, because a piece of the body's enzymic machinery is used to make a toxic substance; if nothing were done to the fluoroacetate, it would be innocuous. It is therefore the opposite of the well known instances of protective synthesis where a potentially toxic molecule has its toxicity much reduced by coupling with glycuronic acid or other such substance. It is what one would like to do with a cancer if a knowledge of its metabolism would show up some difference of which advantage could be taken. It is likely to prove a more general phenomenon, and at least one analogous case has appeared in the insecticides, where a compound initially non-inhibitory to the enzyme cholinesterase becomes so when injected. The real puzzle is how living matter can continuously protect itself against more happenings of this character, and, as always, the deeper the research the more does our respect grow for the conditions under which life becomes manifest.

NOTE. The author is indebted to Sir John Simonsen, Dr Galley, and the Director of Njala Station for the seeds of *Dichapetalum toxicarium*. He also wishes to thank Dr Claude, Dr Palade, and the 'Journal of Histochemistry and Cytochemistry for the micrographs reproduced in figure 4.

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Reaction paths in plant respiration

W. O. JAMES

While much still remains to be discovered about the respiratory mechanisms of particular species of plants in particular circumstances, the general biochemical pattern of plant respiration can now be discerned, and proves to possess a striking resemblance to that found in other types of organism. In this article, Dr James reviews some of the principal reaction-paths that have been established, and assesses their relative importance under various conditions.

The idea that has dominated the biochemical study of plant respiration for some seventy years was first put forward for animal tissues, and began from the observation that many tissues—probably all plant tissues—continue to give off carbon dioxide when they are deprived of oxygen. It was clear that metabolic changes akin to a fermentation went on, at least for a while, in the total absence of oxygen.

It would not be extravagant to regard these anaerobic changes, which include a redox reaction, as a sort of basic respiration, and the additional oxidation in the presence of molecular oxygen as a refinement improving efficiency at the expense of increased elaboration of machinery. It is even possible to regard these two stages as showing an actual evolutionary advance from a primitive condition of life in an airless world to a level made possible by the advent of oxygen. The case has been eloquently pleaded by Oparin [1].

There was, in fact, nothing novel in the idea of anaerobic metabolism by 1878, when Pfeffer applied it to the higher plants. The period coincided with the studies of Pasteur on yeast, and great interest attached to the observation that alcohol appeared to be formed in the tissues. Pasteur himself distilled alcohol from a number of succulent fruits, such as plums, subjected to varying periods of deprivation of oxygen. The question arose whether the alcohol had truly been produced by the mesocarp of the fruit, or whether it might not rather have been formed by epiphytic yeasts. Pasteur thought not, but it is a matter of great difficulty to maintain sterility over so long an anaerobiosis, and Pfeffer and others later expressed doubts about these early experiments. Subsequent investigation has largely aimed at clearing up three points: firstly, the authentic origin of the anaerobic product from plant tissue as distinct from microbial intruders; secondly, the correctness of its identification as alcohol; and, finally, the extent of its formation.

The earliest experimenters sought to exclude alcohol of microbial origin by cutting out deep-seated samples of tissue for analysis. The only plant tissues that can be rigidly sterilized without destroying them are dormant seeds protected by thick non-living coats, and the device has therefore been used of introducing sterilized seeds into sterilized vessels and germinating them in the enclosure. Some oxygen must be present at first or germination fails, but it can be withdrawn after a few days. Recently, the problem has been simplified by the use of antibiotics; streptomycin, if combined with a normal degree of cleanliness of apparatus, will keep the surface of carrot tissue, for example, free from significant contaminations for several days.

The earlier identifications of alcohol in plant tissues depended on volatility, smell, the iodoform test, and the smell of ethyl benzoate. Phillips [2] achieved some improvement by comparing the refractive index of distillates with their dichromate-reducing power, and her results with preparations from barley seedlings agreed to within 3 or 4 per cent. The principal obstacle to satisfactory identification by normal chemical methods lies in the fact that the alcohol is produced in the presence of a large excess of water. Since reaction with 3,5-dinitrobenzoyl chloride to obtain a conveniently characterized ester occurs only in the absence of water, separation and drying become necessary but tedious processes attended by much loss. Adequate quantities of the ester have now been prepared with alcohol derived from barley seedlings, apples, carrots and other plant tissues [3].

The common theory of alcohol formation in higher plants has always been moulded on that for yeast, although other reaction paths are known, for example in *Escherichia coli*. It is assumed that the equation $C_6H_{12}O_6 \rightarrow 2C_2H_5OH + 2CO_2$ will be obeyed, except so far as it may be disturbed by side-processes or accumulation of intermediates.

Its quantitative investigation in higher plants is more difficult than in yeast, because the sugar to be determined is an unknown mixture within the tissues instead of a simple known addition. Only quite recently has the attempt to relate amounts of sugar consumption and alcohol formation been seriously made—or, indeed, become possible with increased refinements in the micro-analysis of sugars. Failing such means, the earlier workers, notably Palladin and Kostychev, concentrated their attention on the relative amounts of alcohol and carbon dioxide formed. Although the ratio 1 : 1 is required by the equation, its occurrence would do very little, without simultaneous knowledge of the loss of sugar, towards proving it. Known biological products of sugar-breakdown, like lactic acid and glycerol, need cause no disturbance in the ratio of alcohol to carbon dioxide. This could quite well result from a trifling side-reaction rather than from the main course of events. As it turned out—rather fortunately—the predicted value of unity was obtained only with a minority of tissues, which included germinating peas and rice, and storage carrots. Other results all showed an excess production of carbon dioxide over that of alcohol, but the causes of this excess are still largely a matter of conjecture.

In 1903, Nabokich [4] found that the alcohol to carbon dioxide ratio for germinating peas lay very close to unity, the values in seven separate experiments varying only from 1·03 to 0·96. He also determined the loss of solids by weighing the dried residues. On the assumption that the whole of this loss was due to breakdown of starch, he was able to calculate the 'hexose' consumption and compare it with the weight of alcohol plus carbon dioxide recovered. The mean of the recoveries fell only 2 per cent short of the calculated mean consumption.

Carrot tissue has been investigated more specifically. Values close to unity have been repeatedly obtained for the molecular ratio of the products, and only the simple, soluble sugars appear to be broken down during two or three days of aseptic anaerobiosis. Recent analyses using the Somogyi technique have shown a loss of sugar, calculated as weight of hexose, little if at all in excess of the recovery of alcohol and carbon dioxide. At the same time it has been found that no considerable amounts of acetaldehyde, glycerol, phosphate esters, lactic acid, or other carboxylic acids accumulate [5]. The anaerobic respiration of this tissue appears, indeed, to be a near approximation to a simple alcoholic fermentation.

It is interesting to find that at least some plant tissues promote a known and relatively simple series of reactions, but this cannot be the whole of the story; some are known to consume other materials besides sugars. Apples accumulate malic acid in the early stages of their development, and steadily consume it during slow ripening in cool storage. Fidler [6] has shown that the rate of consumption is not altered by the absence of oxygen over long periods. The alcohol to carbon dioxide ratio varies considerably, never exceeding unity, and sometimes falling as low as 0·4. The excess carbon dioxide could be more or less quantitatively accounted for by the supposition that malic acid continues to be fully oxidized to carbon dioxide in an atmosphere of nitrogen, but this rather difficult assumption has not yet been substantiated.

The recently published studies of Barker and El-Saifi [7] on potatoes illustrate another type of variation. Carbon dioxide continues to be given off in an atmosphere of nitrogen, but only at a reduced rate. No alcohol appears unless the tubers are cut, sliced, or otherwise damaged, but there is a steady accumulation of lactic acid. The free sugars of potatoes are constantly replenished from the vast excess of starch, and it is unfortunately not possible to determine the actual sugar-loss for comparison with the amount of lactate appearing. It is, however, clear that this accounts for only a relatively small part of the whole anaerobic respiration, because some carbon dioxide continues to come off, and alcohol-soluble solids not yet identified accumulate to about the same weight as the lactic acid. Simultaneous formation of carbon dioxide and lactic acid without alcohol might result from the dismutation

$$2CH_3\,CO\,COOH \rightarrow CH_3\,COOH + CO_2 + CH_3\,CHOH\,COOH$$

as carried on by some bacteria and, it is claimed, by tomato stems [8]. When the potatoes were transferred to nitrogen, the ratio of carbon dioxide and lactic acid productions followed opposite instead of parallel courses. While the rate of lactic acid formation accelerated the rate of carbon dioxide release fell away, and the evidence must be taken to show that the unknown products and the carbon dioxide come not from the above, but from some still unidentified reaction. After prolonged deprivation of oxygen, or if the cells are mechanically injured, the restriction on alcohol-formation disappears and alcohol accumulates

instead of lactic acid. Nevertheless, it clearly cannot be assumed that anaerobic respiration in the higher plants is synonymous with alcoholic fermentation. An attempt to calculate sugar loss from observed production of carbon dioxide by means of the fermentation equation would be subject to evident risks and only fully justified after direct investigation of the tissue in question. These risks have been rather often incurred, and it remains for the future to decide whether justifiably or not.

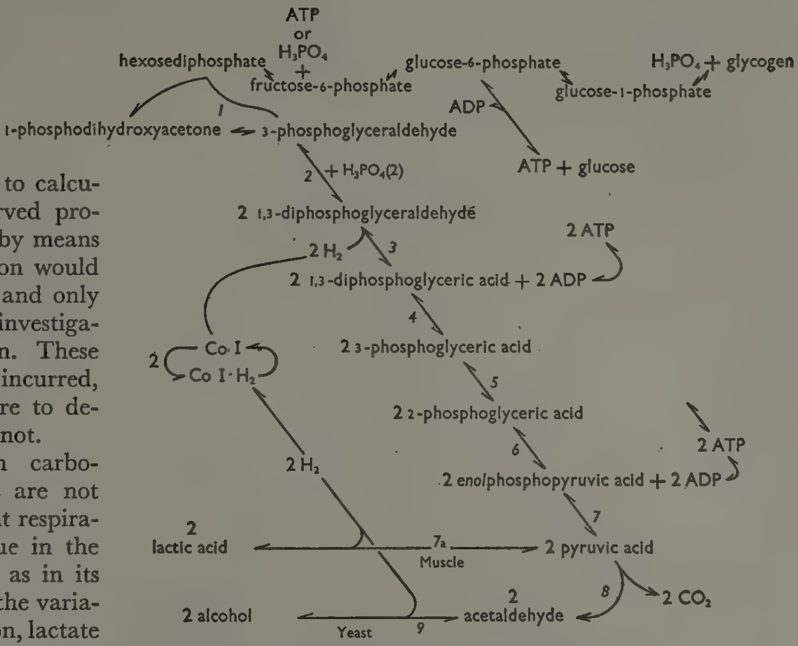


FIGURE 1 – *The Embden-Meyerhof scheme of glycolysis.*

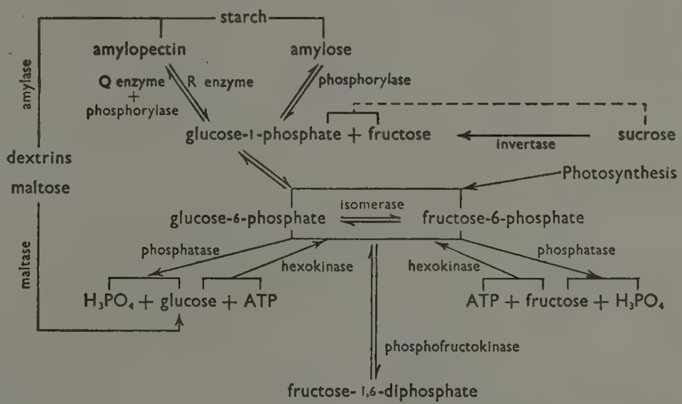


FIGURE 2 – *Reactions leading to the formation of fructose* 1,6-*diphosphate in plant tissues.*

Metabolites other than carbohydrates and plant acids are not normally consumed in plant respiration, and this may be true in the absence of oxygen as well as in its presence. Some at least of the variations of anaerobic respiration, lactate formation in particular, are closely related to alcoholic fermentation and may be regarded as deflections of a common reaction path. So far as carbohydrate-breakdown is concerned—and this is almost certain to be the main process—there appears to be a remarkable similarity of reaction mechanism in organisms of all kinds. However much the final products may be made to differ by side or subsequent reactions, the initial attack adheres to a common type characterized by phosphate catalysis. The details of this complex reaction sequence, as revealed in yeast and muscle, are now too familiar to need description here; figure 1 provides a synopsis. Two stages may be recognized: first the phosphorylation culminating in the synthesis of hexose- (fructofuranose-)1,6-diphosphate, and then the glycolysis ending with pyruvic acid. The carbohydrate phosphorylated may vary; it is commonly either starch or sucrose in the higher plants; more rarely a hemicellulose, a fructosan, or raffinose; even glycosides or fats may be pressed into service by one tissue or another. The range in the saprophytic fungi may be even wider, and, although glucose is the common sustenance of yeast, other carbohydrates also are attacked; among bacteria it would be difficult to set the limits. Whatever the source of the hexose units, the product of anaerobic phosphorylation is likely to be hexose-diphosphate. All the reactions indicated in figure 2 have now been identified in plants.

The kinetic relations within healthy plant tissues are such that hexosediphosphate does not accumulate. It may, however, be caused to do so in cell-free extracts and mushes, especially if they are fed with sugar and adenosine triphosphate (ATP). It would appear a reasonable speculation that the conversion of fructofuranose-1,6-diphosphate to

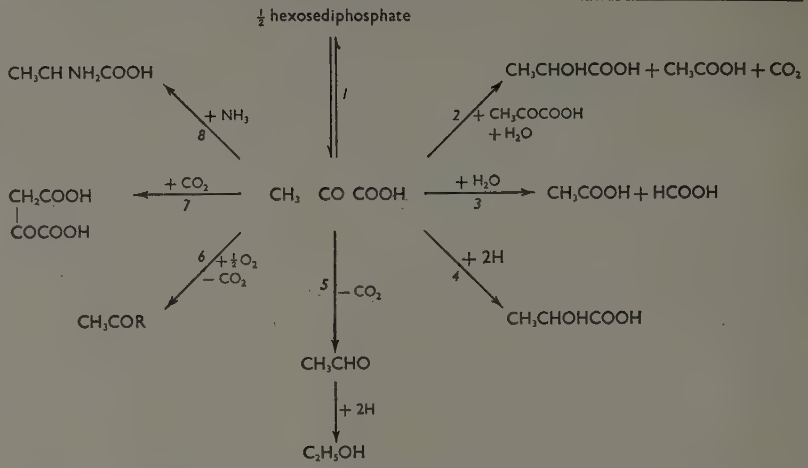


FIGURE 3 – *Reactions of pyruvic acid in biological systems. Reactions* 1, 4, *and* 5 *occur in plants anaerobically;* 6 *in aerobic respirations;* 7 *in* CO_2*-fixation by plants in the dark;* 8 *probably in nitrogen metabolism.*

pyruvic acid is the most uniformly managed of all biological processes. There is a type of organism, exemplified by *Trypanosoma evansi*, that produces pyruvic acid in the conventional way, but, having done so much, troubles itself no further. This interesting economy of metabolic effort is possible only to a parasite living in the bloodstream of a host that will dispose of the inconveniently reactive pyruvate. In more normal organisms the consequences of pyruvic acid formation must work themselves out internally.

The formation of pyruvic acid in respiring barley tissues was shown in 1940 [9]. It appeared in isolable amounts only after its consumption had been retarded by application of an enzyme block, suggesting that formation and disposal were both going on during normal glycolysis. Evidence for the reaction path indicated in figure 1 has since been patiently accumulated [10]. In 1953 Axelrod and Bandurski [11] showed the presence in pea meal of phosphoglyceryl kinase, the enzyme catalysing the reaction 1,3-diphosphoglyceric acid + adenosine diphosphate ⇌ 3-phosphoglyceric acid + ATP. This enabled them to state that all the enzymes of the Embden-Meyerhof scheme of glycolysis have now been shown to be present in higher plants. The essential coenzyme-I (diphosphopyridine-nucleotide) and adenosine phosphates have also been extracted. Though the molecular structures of the higher plant products have not yet been established, functionally they appear to be interchangeable with those from yeast. It can further be added, as a result of experiments with inhibitors such as iodoacetate, fluoride, and aromatic sulphonic acids, that the reactions appear to proceed in the living plant tissues, and that the scheme is actually as well as potentially operative.

The presence of pyruvic acid poses a metabolic problem that has many possible solutions; some of them are indicated in figure 3. The answer most favoured by the higher plants in the absence of oxygen appears to be decarboxylation followed by reduction, leading through acetaldehyde to alcohol (5). Suppression or control of the decarboxylation leads to the formation of lactic acid (4). This, the standard reaction in muscle, occurs also (as mentioned) in potatoes, with a ready relapse to alcohol formation in trauma. Lactic acid is known to be formed in other plants, and the extent of its participation in their anaerobiosis is ripe for investigation. Other anaerobic disposals of pyruvic acid, such as occur in some bacterial fermentations, have not yet been observed in higher plants.

The effect of oxygen upon the organized reaction-system of glycolysis is complex and only partially understood. There are two main types of response when tissues are transferred from an atmosphere of nitrogen to one of air, and these are diagrammatically summarized in figure 4. The unbroken line represents the rate of release of carbon dioxide from storage carrots kept in nitrogen. On return to air they show a direct readjustment to their original rate. Potatoes, on the other hand, show a massive increase of carbon dioxide production, which settles back to the normal air line only after a large amount of additional carbon dioxide has come off (figure 4, broken line). As described above, carrots in an atmosphere of nitrogen accumulate only alcohol, which they are unable to oxidize; once formed, it persists in the tissues, even in air. The lactic acid formed by potatoes, on the other hand, is rapidly oxidized by them when oxygen becomes available. While this is going on, pyruvic and other plant

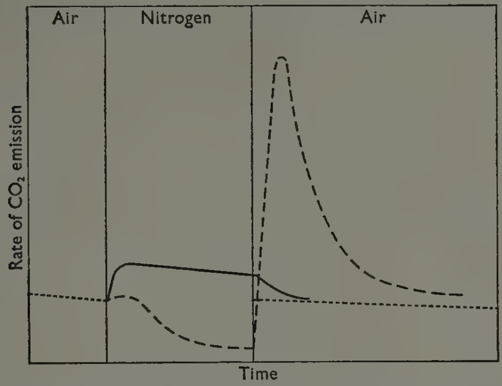


FIGURE 4 – *The rate of CO_2-emission during transfers between air and nitrogen. . . . . . adjusted rate in air; ——— carrots removed to nitrogen and back to air; - - - - - potatoes removed to nitrogen and back to air.*

acids accumulate to a higher concentration than usual, and are gradually fully oxidized to give the additional carbon dioxide that comes off. The difference of response does not depend upon the reduction-product formed. Some tissues are able to oxidize alcohol, and are then likely to show a post-nitrogen effect like that of potatoes.

The inability of some plant tissues to oxidize alcohol gave rise early to the suggestion that oxidation must intervene at earlier stages of glycolysis. Direct oxidation of sugars to C_6-acids has never been shown to happen in the higher plants, and its well known occurrence in the mould fungi may be exceptional even within that group. A good deal of familiar physiological and biochemical evidence goes to suggest that oxidation modifies glycolysis rather than supersedes it by directly oxidizing sugars. The almost invariable oxidizer of glycolysis products is coenzyme-I, with the occasional substitution of coenzyme-II (triphosphopyridine-nucleotide). The reactions are catalysed by dehydrogenases, which are highly specific towards the hydrogen donors after which they are named, and absolutely specific towards the acceptor. In some plant tissues hydrogen may be transferred from triosephosphate either to coenzyme-I or to coenzyme-II, but the two reactions are catalysed by separate dehydrogenases [12]. Glycolysis products likely to be oxidized by coenzyme-I are indicated in figure 5. The oxidation of triose phosphate occurs anaerobically, when the catalytic amounts of coenzyme-I present are reoxidized by transfer of the accepted hydrogen to acetaldehyde or pyruvic acid. When oxygen is introduced it becomes a preferred hydrogen acceptor, and the production of alcohol and lactic acid is retarded or, at above some 5 per cent of oxygen, entirely suppressed. Lactic and alcohol dehydrogenases catalyse their anaerobic reductions; it is doubtful whether they ever get the chance in healthy tissues to catalyse the reverse oxidations, except temporarily after a previous nitrogen treatment. The deflection of the hydrogen transfer, or more exactly the electron flow, to oxygen does not change the oxidation product of the triosephosphate, and the reaction-chain continues unaltered at least as far as pyruvic acid.

The aerobic fate of pyruvic acid and acetaldehyde has posed one of the most difficult problems of plant metabolism. The favourite solution at present is the supposition that pyruvic acid is oxidatively decarboxylated with the formation of acetyl groups in lieu of acetaldehyde. The condensation of acetyl with oxaloacetic acid initiates the Krebs cycle of reactions, in which an acetyl equivalent is totally oxidized and oxaloacetic acid continuously regenerated (figure 6). It has recently been found possible to centrifuge out from plant tissues particles about 1 μ in diameter that may be identical with the cytologists' mitochondria. These vigorously catalyse the oxidation of pyruvic acid, and it has been convincingly shown by a variety of techniques that they do this by the Krebs cycle of operations [13]. When, for example, the particles are incubated with ^{14}C carbonyl-labelled pyruvic acid, $CH_3.^{14}CO.COOH$, and any one of the cycle-acids is added as a trap, this rapidly becomes labelled also [14]. It is probable that some at least of the necessary enzymes exist only in the particles, and that the cycle could not operate in phases of the protoplasm outside them.

The evidence is now good that the cycle actually

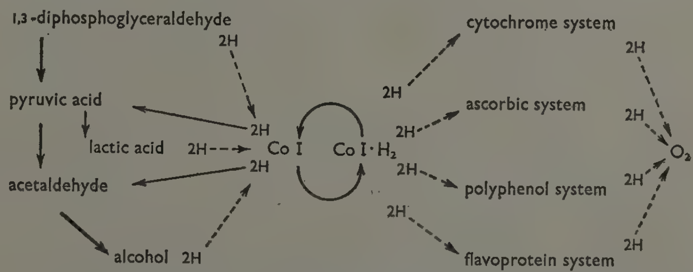


FIGURE 5 – *Reduction and oxidation of coenzyme-I. Thin black arrows indicate anaerobic transfers of hydrogen, arrows with broken lines indicate aerobic transfers.*

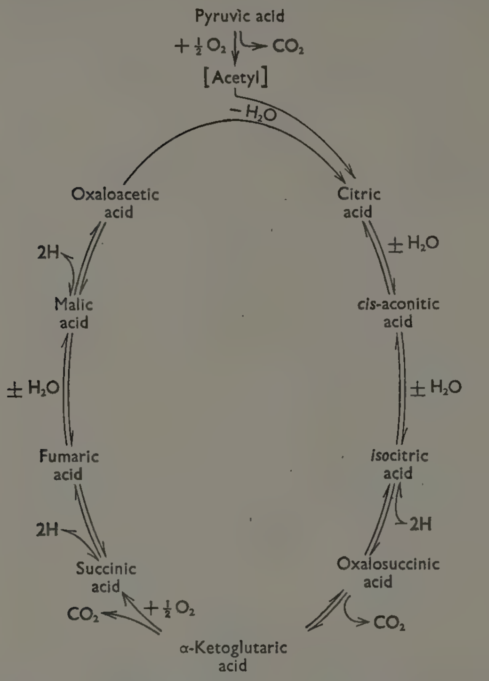


FIGURE 6 – *Principal reactions in the oxidation of pyruvic acid by the Krebs cycle.*

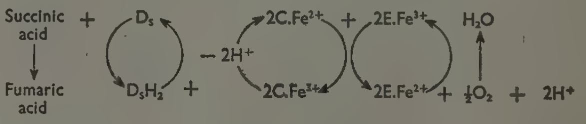
operates in at least some plant tissues, and that it revolves fast enough to account for their respiration. This hypothesis is so seductive that objective appraisal is not easy. Not only may it dispose of an otherwise awkward respiratory situation, but it also accounts for the presence of many of the plant acids and, perhaps most appealing of all, it forges a credible link between carbohydrate and protein metabolisms by providing the most suitable α-keto acids for amination.

Most of the available evidence points, strictly speaking, only to the occurrence or possibility of the reactions, and gives no indication whether they go fast enough to provide a major respiratory pathway. They might represent an important metabolic sequence even if too slow to catalyse respiration, and, according to Krebs [15], this situation arises in yeast. Among the higher plants there is a dilemma, unresolved at the moment of writing, that may lead to the same conclusion for some plant tissues. Hackett and Simon [13] have isolated a particulate preparation from *Arum* spadix that vigorously promotes the oxidation of pyruvic acid, apparently by the Krebs mechanism; yet the respiration of the same tissue presents characteristics that make it very difficult to believe that it is catalysed by the same system [16].

Among higher plant tissues that may be cited as using the Krebs cycle as a respiration mechanism are spinach leaves [17] and germinating barley embryos [18]. The respiration of the latter is accelerated by additions of succinic, fumaric, and α-ketoglutaric acids, especially if accompanied by pyruvic acid after about 20 h of previous starvation. Malonic acid inhibits at low *p*H, and subsequent addition of fumaric acid largely restores the oxygen consumption. Fluoroacetic acid also inhibits heavily and causes the accumulation of citric acid in the tissues by jamming the initial stages of the cycle, as elucidated by Peters with animal preparations. 2,2′-Dipyridyl also strongly inhibits the respiration of these tissues. It has no effect on the anaerobic stages or on the oxidation enzymes, but does inhibit aconitase, the enzyme catalysing the equilibrium between citric, *cis*-aconitic, and isocitric acids in the cycle. It has been shown with spinach leaves that malonic acid poisoning leads to the accumulation of succinic acid [17]. Since, when these things happen, the respiration of the tissues is heavily curtailed, it is reasonable to assume that the reaction cycle is here an effective respiratory agent.

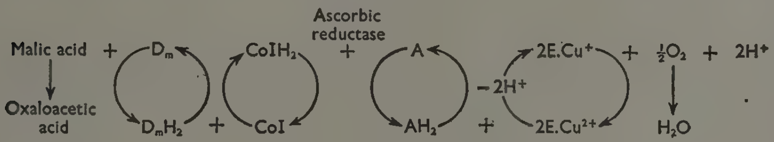
Transfer of hydrogen from the cycle-acids is more variable in its direction than is transfer from the glycolytic donors. Malic dehydrogenase transfers hydrogen to coenzyme-I; isocitric dehydrogenase prefers coenzyme-II, and succinic dehydrogenase uses cytochrome. All three occur only in catalytic amounts, and continuous oxidation requires their regeneration by electron-transfer to atmospheric oxygen. The four redox systems in figure 5 are known to exist in plants and would appear to be capable of catalysing these transfers; they have in fact been induced to oxidize the reduced coenzymes after extraction.

The shortest oxidation chain, and one of the best authenticated as occurring in plants, catalyses the oxidation of succinic acid to fumaric by the cytochrome system, which apparently eliminates the coenzymes. It may be represented



writing D_s for succinic dehydrogenase, $C.Fe^{2+}$ for reduced cytochrome, and $E.Fe^{2+}$ for reduced cytochrome oxidase.

The oxidation of malic acid by coenzyme-I, and that of isocitric acid by coenzyme-II, introduce a further enzyme, cytochrome reductase, which catalyses the transfer of electrons from the coenzyme to a cytochrome. Similar oxidation chains have been extracted from plants and assembled *in vitro* using ascorbic acid and oxidase, or a polyphenol and polyphenol oxidase. Malic acid oxidation through the ascorbic system as extracted from plants may be written



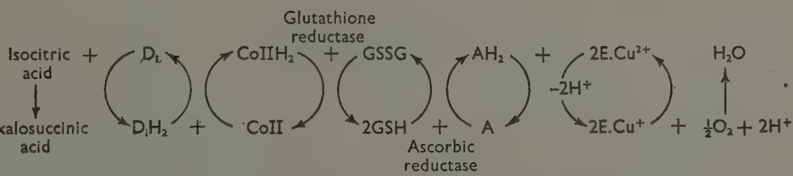
Ascorbic acid is here written AH_2 and reduced ascorbic oxidase as $E.Cu^+$.

The possibility of reconstructing these systems *in vitro* does not necessarily prove their activity inside the tissue. According to present information, the most important redox chain in plant respiration is the cytochrome system. Convincing evidence of its activity in seedling and some other tissues has been obtained, and it probably catalyses at least four-fifths of their respiratory oxygen consumption. This conclusion rests mainly on the evidence that the system may be extracted from such tissues, that the characteristic absorption bands may be seen to fluctuate appropriately with the redox conditions imposed on the tissues, and that the respiration is heavily inhibited by dilute cyanide. Finally, and most conclusively, the respiration suffers an inhibition by carbon monoxide which is reversed by visible light of short wavelength.

Present information is, however, rather scanty, and it would be rash to assume that these deductions may be applied to all plant tissues, especially as some of the tissues already examined appear to provide exceptions. There is no convincing evidence at present that any plant tissue utilizes the polyphenol system in its normal respiration: the numerous claims made at one time on its behalf rested on evidence that has since proved to be insufficient. The flavoprotein and ascorbic acid systems may, however, operate.

The sterile spadix of some aroid inflorescences is noted for its rapid respiration, leading to the production of much heat and a rise of temperature around the flowers enclosed in the spathe. This is a very exceptional tissue, and investigation of its respiration has led to unusual results. Its very rapid respiration cannot be inhibited by cyanide, azide, carbon monoxide, or malonic acid, that is to say by any of the inhibitors to which cytochrome oxidase and its associated succinic dehydrogenase are particularly susceptible. No cytochrome oxidase can be extracted by the usual methods, and the other metallo-enzymes, polyphenol and ascorbic oxidases, seem to be absent also. A crude preparation of an autoxidizable flavoprotein has been obtained [16], though attempts at purification have not yet succeeded. Since the activity of homogenates is greatly increased by addition of riboflavin, and the respiration of the tissues is markedly sluggish towards oxygen, it is probable that the role of the terminal oxidase is here filled by a non-metallic flavoprotein enzyme.

Numerous experiments carried out at Oxford indicate that the meristems of young barley roots soon fail to produce the cytochrome system found in the embryo. Inhibition by cyanide persists, but all the other criteria of cytochrome oxidase activity disappear after the first few days, and in their place a marked susceptibility to 'dieca' (sodium diethyldithiocarbamate) develops. The known facts are most readily explained on the assumption that the respiratory oxidations are carried through this phase by the ascorbic system. Malic acid can be oxidized by it through coenzyme-I, and recent results [19] indicate that isocitric acid, whose dehydrogenase requires coenzyme-II, may be oxidized by way of glutathione (GSH):



So far, the ascorbic system has not been linked with the oxidation of succinic acid, and it is uncertain whether the entire Krebs cycle of oxidations can be promoted by it. Collateral experiments with wheat and rice indicate a steady adherence to the cytochrome system; the remarkable

oxidase-shunt operated by the young root-tips of barley, while maintaining a uniform rate of respiration, appears to be characteristic of barley itself. The mechanism of respiratory oxidation in mature plant-tissues is still very uncertain.

The oxidations of plant respiration, like those of animal tissues, promote the phosphorylation of adenosine diphosphate (ADP) to adenosine triphosphate (ATP) with a consequent retention of transferable energy. The isolated 'mitochondria' perform this reaction while oxidizing pyruvic acid. It has not yet been possible to determine the full amount of phosphate esterified, because of active hydrolysing enzymes also present. It exceeds, and perhaps greatly exceeds, one phosphate per atom of oxygen consumed, equivalent to twelve or more per hexose molecule, as compared with a net gain of two or three during anaerobiosis. Glycolysis provides enough ATP by the dephosphorylation of 1,3-diphosphoglyceric acid and *enol*phosphopyruvic acid to phosphorylate fresh hexose and maintain the cycle (figure 7). The net gain of ATP that might be applied to other cell requirements is small, and it is notorious that growth and synthesis—indeed, all the most energetic cell activities—come to a stop without oxygen; even mere maintenance of the system becomes precarious before long. When, with the help of the oxidation trains of the cell, oxygen replaces pyruvic acid or acetaldehyde as electron acceptor, the oxidation, instead of reduction, of pyruvic acid and its products greatly increases the amount of ATP formed for a given hexose consumption. The proportion needed to continue the phosphorylations of glycolysis becomes less, and the excess ATP is available to promote the many syntheses known to depend upon its energy, including amidations and the peptide linkages that build the primary valency chains of proteins; perhaps, indeed, growth syntheses in general.

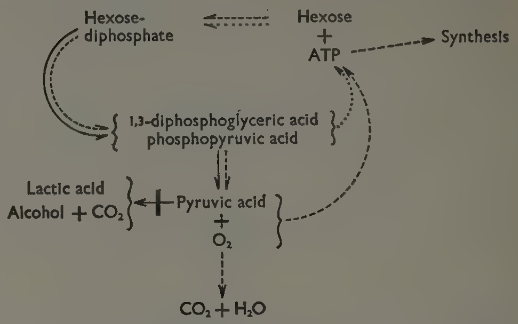


FIGURE 7 – *The effect of oxygen in the phosphorylation cycle. Anaerobic processes are shown by solid or dotted lines, aerobic by broken lines. The dotted lines indicate that the process is slower than its aerobic equivalent.*

Comparing what is known of plant respiration with the corresponding processes in other types of organism, one cannot help being impressed by the fundamental unity of biochemical procedure. Almost without exception carbohydrates are phosphorylated, fructofuranose-1,6-diphosphate is split to pyruvic acid, and pyruvic acid is wholly or partially degraded to carbon dioxide. The first stages may be regarded as an activation and the last as the delivery of energy from the vantage-point thus obtained.

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Book reviews

CLASSIFICATION OF FUNGI

Flore analytique des champignons supérieurs, *by R. Kühner and H. Romagnesi. Pp.* 556, *with* 677 *text figures. Masson et Cie., Paris.* 1953. *Paper cover, fcs* 7010; *bound, fcs* 7970 *net.*

Considering the eminence and international reputation of the authors of this work, it is not surprising that it is difficult to describe its scientific value without resort to superlatives. The taxonomic treatment of some 2500 species and varieties of fungi included under the headings agarics, bolets, and chanterelles is essentially based on many years of personal observation, though the authors have been influenced by the generally accepted views of other mycologists. The text is divided into clearly defined sections, which greatly facilitates specific determination. It is illustrated by numerous small, but delightfully drawn, sketches of fungi or their parts. In addition to the main taxonomic treatment, some fifty pages are devoted to supplementary information on such things as poisonous fungi, investigation technique, and colour concordance. There are a very full glossary and an adequate index.

Some criticism is, however, inevitable. In starting with Fries' *Epicrisis* of 1836 instead of his *Systema* of 1821, the authors show a light-hearted indifference to the rules of international nomenclature; this, however, might be regarded as not so much a matter for criticism as for congratulation. New species, new varieties, and new names appear with startling frequency, but with no Latin diagnosis—not even a description. The manner in which Friesian genera have been shuffled and re-dealt is often bewildering, in spite of the indispensable table of comparison between Friesian classification and the authors' rearrangement. The division of genera into so-called 'natural' groups is often dependent on very detailed microscopic examination, as for instance in the genus *Tricholoma*, where the primary separation into groups is based on such characters as amyloid spores and hyphal clamps.

No criticism, however, could seriously detract from the scientific value of this excellent work. Its great merit is that it does exactly what it sets out to do and does it remarkably well. It is one of the outstanding contributions of modern times towards the solution of the problems inherent in the taxonomy of the fungi.

W. H. WILKINS

GENETICS

The Facts of Life, *by C. D. Darlington. Pp.* 467. *George Allen and Unwin Limited, London.* 1953. 35*s. net.*

Professor Darlington's book starts with an amusing history of the science of heredity, from the Bible to Darlington, with excursions to telegony, the Kammerer case, and Lysenko. It builds up a *Weltanschauung* explaining the riddles of the universe in terms of chromosomes and genes, and ends with a new gospel designed to cure scientifically the evils of our time. Thus, problems old and new—cancer, evolution, language, criminality, race, the classes in human society, divorce and homosexuality, Freud, the belief in immortality, the rise and fall of civilization, and the indeterminacy principle—are solved by saying that it is all due to the genes. The principle that what is genetically determined is rather a norm of reaction than manifest characters seems to be by-passed in a rather cavalier fashion.

The Bachs, the Bernoullis, and the Darwins 'owed their gifts to heredity' (p. 275). So be it: but Beethoven, son of a notorious drunkard, was highly undesirable by all eugenic standards, and Goethe was the son of the remarkably mediocre *Rath* of Frankfurt and ancestor of an equally inconspicuous progeny. How, then, is Darlington's remedy for the ailments of our time going to work, to wit, that the State should control fertilization (p. 357)? There are a 'diagram of love' (p. 327) and, somewhat lacking in taste in the context, a table on the fertility of bulls as established by the results of artificial insemination (p. 337). The genetic character expressed by the table (classes from 0 to 3000+ cows fertilized per bull per annum—the human counterpart of the latter, class VIII, 'being responsible for the greatest poetry,' p. 341) 'decides the success or failure of a marriage both from the view of the individuals concerned and of the community' (p. 344). 'We can now understand the modes of action (of genes, chromosomes, plasmagenes, and viruses) in heredity and development, in infection and immunity, in the animal body and even in the human mind' (p. 389). Can we? We know that genes in the mould *Neurospora* interfere in the production of certain enzymes, that certain amino acids are responsible for the eye colour in *Drosophila*, and the like. Who has the faintest idea of how chains of nucleic acids, called genes, are capable of producing even the organization of a fly or a mouse, not to speak of the musical genius in the Bach family or the criminality of the Lange twins? 'The materials of heredity contained in the chromosomes are the solid stuff which ultimately determines the course of history' (p. 404). So simply explained are human affairs!

The impact of genetics on modern science, pure and applied, on medicine and the social sciences, can hardly be over-estimated. It seems doubtful, however, whether over-simplifications and half-truths will do much service for its popularization. Professor Darlington is, however, highly successful in giving us a mythology of the gene, where those little nucleic acid dots play a role similar to that of fairies, furies, and gods in the times of old.

LUDWIG VON BERTALANFFY

FOAMS

Foams: Theory and Industrial Applications, *by J. J. Bikerman, with chapters by J. M. Perri, R. B. Booth and C. C. Currie. Pp.* 347, *with half-tone and line illustrations. Reinhold Publishing Corporation, New York.* 1953. 80*s. net.*

This book is a unique compilation of information of all kinds on foams, and as such should be valuable to a wide circle of readers, particularly to industrialists whose processes either depend upon foams or are troubled with unwanted foams. There are chapters on the structure of foams, their mechanical, electrical, and optical properties, their rate of drainage, and the use of foams for separating constituents of solutions; also accounts of foams suitable for fire-fighting and methods of testing their efficacy, of the froth-flotation process for mineral separation, and of substances with foam-destroying properties. There are copious references to original papers and patents—indeed, some parts of the book are mainly a survey of patent literature. Although there is a good deal of theory scattered throughout the

book, it is neither well co-ordinated nor original, and the chapter on the theory of foams is so badly out of date that it ignores most of the work done on the structure of surface films on water or aqueous solutions since 1900. As a compendium of useful information, this book has considerable value; as a contribution to the difficult science of foaming it is of minor importance.

N. K. ADAM

INVERTEBRATE PALAEONTOLOGY

Traité de Paléontologie, *publié sous la direction de Jean Piveteau. Volume III. Les formes ultimes d'invertébrés: morphologie et évolution. Onychophores—Arthropodes—Échinodermes—Stomocordes. Pp. viii +* 1063, *with* 1274 *figures and* 17 *plates. Masson et Cie., Paris.* 1953. *Paper covers, fcs* 9600; *bound, fcs* 10 320 *net.*

Sixty-one years ago K. A. v. Zittel completed his famous 'Treatise on Palaeontology' (*Handbuch der Paläontologie*), which represented his life's work. Some time ago Professor Jean Piveteau of the Sorbonne undertook the publication of a *Traité de Paléontologie* in seven volumes, and, within a year after the publication of the first two volumes, the third volume is now ready. It deals with highly organized invertebrates. The years that have passed since the publication of Zittel's work have brought a considerable widening of relevant knowledge and a deeper insight into the natural inter-relationships of the organisms. This is particularly noticeable in this third volume. One of the most striking changes in the system of classification concerns the position of the now extinct Graptolites. Originally considered to be plants, and classified by Zittel among the Hydrozoa, they have now been recognized as relations of the Pterobranchia, and thus belong to the Stomochordates, occupying a position intermediate between the Echinodermata and the Chordata.

Zittel's treatise was entirely his own work and as such of a strikingly uniform character. A command of the whole field of palaeontology is today beyond the capacity of one worker. The editor therefore secured the co-operation of a number of French palaeontologists, to whom he allocated the various sections. The contributors to the third volume are: F. M. Bergounioux, L. Cuénot, C. Dechaseau, M. Deflandre-Rigaud, N. Grekoff, P. Hupe, D. Laurentiaux, J. Piveteau, J. Roger, H. and G. Termier, G. Ubachs, and G. Waterlot. They were apparently given complete freedom in the execution of their task, and thus a symposium of great variety has resulted. Illustrations are plentiful and of excellent quality throughout.

Emphasis lies on zoology; stratigraphy seems to have been neglected on occasions. Systematics mostly goes as far as the genera. The bibliography is valuable, though by no means complete. The work will be an indispensable aid to palaeontological research.

EMIL KUHN-SCHNYDER

DICTIONARY OF ENGINEERING

Dizionario d'Ingegneria, *edited by Eligio Perucca. Volume III,* FOS–MOS. *Pp. viii +* 1043, *with* 2100 *figures and four plates. Unione Tipografico-Editrice Torinese, Turin.* 1953. *Lire* 12 000.

This volume must have been awaited with impatience by everybody, in Italy or elsewhere, who has had the opportunity of consulting its two predecessors, reviewed in the April 1953 issue of ENDEAVOUR. This dictionary is a veritable mine of up-to-date information and a collection of little monographs written by experts, some of which will be read with profit not only by engineers; one would like to mention in particular that on measurement and systems of units. Cross-indexing is one of the most successful features, and makes it possible readily to extract the desired information, even if one has not been wise or lucky enough to guess directly the entry containing it.

Of course, different readers, with different biases, will find that not enough has been said about their pet subjects—for instance, in the case of the reviewer, photoconductivity. Also the standard of knowledge required from the user does not appear to be completely uniform. Few references are given, and it is felt that more help should have been provided for those requiring more detailed information. A feature very helpful to non-Italian readers would have been the universal decimal classification of the various entries—but this would have been a major undertaking in itself.

The illustrations are excellent, and the production generally is very good; hardly a misprint has been noticed. This work will become the authority on Italian technical terms in the field of engineering, and the editor is to be congratulated again for this most unselfish labour so brilliantly carried out.

L. PINCHERLE

CHROMATOGRAPHY

Chromatography: a review of principles and applications, *by E. Lederer and M. Lederer. Pp. xviii +* 460. *Elsevier Publishing Company, Amsterdam.* 1953. 60*s. net.*

This work, a revised edition of two monographs previously published in French, is a useful addition to the literature of chromatography. It represents the first attempt—and a successful one—at a comprehensive review of the method as a whole since it has become widely used. It has two defects inherent in any undertaking of this kind. The first is that the choice of literature references is subjective; although some two thousand publications are cited, these represent only a fraction of the total. To make a universally acceptable choice is impossible, but nevertheless the authors offer the reviewer little scope for serious criticism; the only point to which it is, perhaps, worth while to draw attention in this connection is that there is no mention of the paper chromatographic work of Liesegang, which deserves to be better known than it is. The second inherent defect is that, like all textbooks dealing with a rapidly developing subject, it became out of date even while it was in the press. It is therefore to be hoped that having put all chemists greatly in their debt by successfully distilling the essence of chromatography the authors will continue the process by offering successive editions at not too long intervals.

A minor point of criticism, which, however, in no way detracts from the practical value of the book, is the reiteration of the statement that Tswett was the originator of chromatography. While none would seek to belittle Tswett, who did outstanding work and may have been an independent discoverer of adsorption column chromatography, the perpetuation of this story does a great injustice to the memories of such earlier pioneers in the same field as Matteucci, Goppelsroeder, Thomson, Way, Reed, Nasse, Engler, Boehm and, above all, the American petroleum chemist D. T. Day.

The preparation of such a valuable work of reference must have been a very great labour, but labour well repaid by its usefulness. The book is concisely written and contains an immense fund of information on all branches of chromatography; must be looked upon as the standard work on the subject. It can be strongly recommended and should be possessed by, or readily available to, all chemists.

T. I. WILLIAMS

THOMAS YOUNG

Thomas Young, Natural Philosopher, 1773–1829, *a biography by the late Alex Wood, completed by Frank Oldham. Pp. xx + 355. Cambridge University Press, London.* 1954. *30s. net.*

This handsome volume is a worthy tribute to one of the greatest of British natural philosophers. A native of Milverton in Somerset, Thomas Young very early gave signs of exceptional intellectual powers; he could read with considerable fluency at two years of age, and before he was four he had read the whole Bible through twice. The precocity was not sterile and fleeting, but developed into a steady capacity for the rapid assimilation of knowledge, which, backed by a typically Quaker habit of industry, soon made Young one of the most learned men of his time. His interests were remarkably wide, and the range and depth of his original investigations have not often been paralleled. He shared with Champollion—whom he quite probably anticipated—the honour of having been the first to decipher Egyptian hieroglyphics; he suggested the wave theory of light; he effectively established the science of physiological optics; he was an accomplished philologist; and he was superintendent of the 'Nautical Almanac' and secretary of the Board of Longitude. This does not by any means exhaust the list of his achievements, but it serves to illuminate the versatility of his genius.

The late Alex Wood collected material for this biography over more than forty years, in the scanty leisure allowed him by his social work and by his duties as Tutor of Emmanuel College, Cambridge, and university lecturer in physics. It is a model of what a biography should be; unfortunately Wood did not live to finish it, but the task has been very well completed by Mr Oldham. The book is excellently produced and illustrated, and is enriched by a memoir of the author by Canon C. E. Raven; this last feature will be particularly welcome to those Cambridge men who profited not only from Alex Wood's inspired teaching but from his warm personality.

E. J. HOLMYARD

RECENT ORGANIC CHEMISTRY

Progress in Organic Chemistry, Vol. 2, *edited by J. W. Cook. Pp. 212. Butterworths Scientific Publications, London.* 1953. *42s. net.*

The six chapters in this book are all written by authors who are actively contributing to the rapid progress now taking place in certain sections of organic chemistry. These concise reviews will be of the utmost value to all whose research work bears any relation to the subjects under discussion. Those whose interest is of a more general nature will be stimulated to consult the original papers, to which numerous references are provided.

With a few exceptions in one chapter the literary style is particularly good, misprints are almost absent, and the infectious enthusiasm of the authors is clearly revealed. This has led in one section to the somewhat excessive, though understandable, use of such terms as admirable, brilliant, elegant, and excellent in describing various researches.

The first impression, that possibly too much space is allotted to the three closely related themes, triterpenes, cortisone, and carcinogenic hydrocarbons, is entirely dispelled by the interesting treatment, and the decision to include these subjects is amply justified.

Even the non-specialist must be continually delighted by the impact of theory on experiment and by the application of unusual reagents or reactions and of modern physical methods. A few instances may be cited —the microbiological hydroxylation of steroids on the important carbon atom 11, and the use of $-6{:}6'$-dinitrodiphenic acid for the resolution of ($\pm$) anabasine, of bismuth oxide for the oxidation of acyloins, and of oxygen adsorbed on active charcoal in the study of pyridoxamine. In conclusion we may mention that, like Volume I, this production is a happy instance of international cooperation.

FREDERICK CHALLENGER

CONTINENTAL CLIMATES

The Climates of the Continents, *by W. G. Kendrew. Fourth edition. Pp. 607. Oxford University Press, London.* 1953. *50s. net.*

When this book was first published in 1922 it almost at once became a standard work, and from that time to the present it has remained the first book in the field to be consulted by student and teacher alike. The title aptly describes the contents: the two introductory chapters, dealing generally with climatic data and world pressure and wind systems, occupy only fifteen pages. Chapter III plunges straight into the climate of Africa, taking first the continent as a whole and then the main countries or regions. The same sequence is followed with each continent in turn, with half a dozen pages of temperature and precipitation statistics at the end of each continental section.

The third edition appeared in 1937 and had been reprinted thrice before the appearance of this fourth edition. The present edition is almost a new work: it has been revised throughout, greatly enlarged, and entirely reset. The general climatic features have been restated in terms of modern air-mass meteorology and fronts. Though the tables suggest an undue emphasis on average monthly temperatures and rainfall, this is counteracted by the many vivid little descriptions of local weather and climate in the text—often culled from the reports of observant non-scientific residents. The continent of Antarctica now has a chapter to itself, but not the Arctic, which is not a continent. The selection of regions remains unsystematic, dictated by availability of material or the author's own interests. Thus North America is treated as a whole, followed by a chapter on the climatic regions of Canada and one on California. It remains a good book with a long life of continued usefulness ahead.

L. DUDLEY STAMP

COLLAGEN

Nature and Structure of Collagen, *edited by J. T. Randall, assisted by Sylvia Fitton Jackson. Pp. ix + 269. Butterworths Scientific Publications, London.* 1953. *42s. net.*

This volume is the published version of papers given at a two-day meeting convened by the colloid and biophysics committee of the Faraday Society at King's College, London, in March 1953 —actually twenty-five papers leavened by nine suitably spaced discussions, and finally rounded off with an excellent twelve-page bibliography. The result matches collagen itself in showing marked variations—some papers and discussions are good, while others are not so good—but that is only to be expected in a conference of this sort, especially on a topic of such complexity. Perhaps it would be fair to say that not a high proportion of the material presented is altogether new in the eyes of the protein addict, but for those who are entering the field or who would like to see how things are going, this book can certainly be recommended. Almost

every side of the collagen problem is dealt with to some extent, from orthodox histology to molecular configuration, as well as by techniques up to the very latest. It is a friendly book, too—an important asset with a subject that is everybody's business; for the collagen group rests on a master plan that accounts for nominally half the fibrous proteins. And particularly we in Britain should constantly bear in mind that collagen is not merely the stuff of the leather industries: it is also, and much more emphatically, the raw material of that great composite human burden, the so-called rheumatic diseases.

W. T. ASTBURY

GUIDE TO THE MOON

Guide to the Moon, *by Patrick Moore. Pp.* 224, *with* 12 *plates*, 13 *figures, and map. Eyre and Spottiswoode Limited, London.* 1953. 16*s. net.*

The Moon is our nearest neighbour in space, and much detail can be seen on its surface with even a small telescope. Its observation is consequently much favoured by amateur observers possessing telescopes of moderate size, who have contributed greatly to the detailed knowledge of lunar topography.

Mr Moore, who is an assiduous lunar observer, has summarized in this book the historical progress of our knowledge of the Moon and its present state. The book will be particularly useful to owners of small telescopes who wish to study the Moon in greater detail. The observation of the detailed topographical structure is complicated by the changing appearance with changing conditions of illumination as the phase and librations of the Moon change. I feel that considerable caution is needed in accepting reports of changes in appearance, and also of long-continued obscuration of features by mists. Though it is not impossible that the Moon may have an extremely thin atmosphere of heavy gases, there is no conclusive proof that it has; Mr Moore has been too ready, in my opinion, to assume the existence of an atmosphere. The evidence for the meteoritic origin of the ring craters has been much strengthened in recent years. Mr Moore discards this theory without adequate discussion and puts forward a highly improbable theory, which does not adequately account for the bright rays.

The later chapters of the book deal with the question of the possibility of life on the Moon and the problems of space travel to the Moon. There are several useful appendices, including a description of the principal lunar features.

H. SPENCER JONES

LIFE OF CARDAN

Cardano, the Gambling Scholar, *by Oystein Ore; with a translation from the Latin of Cardano's* Liber de Ludo Aleae, *by S. H. Gould. Pp. xiv* + 249. *Princeton University Press, Princeton; Geoffrey Cumberlege, London.* 1953. 25*s. net.*

As a physician, Cardan established a European reputation comparable with that of Vesalius. As a mathematician, too, he was among the most eminent of the sixteenth century, and his *Ars Magna* is regarded by many as the first mathematical work to go decisively beyond the limits established by the Greeks. Although the present work contains much information, very readably presented, about Cardan's life generally, and his somewhat questionable dealings with his fellow mathematicians, its principal interest lies in its account of his application of mathematics to the even then widely prevalent vice of gambling. The last quarter of the book is a translation of his *Liber de Ludo Aleae*, which contains the first serious study of the theory of probability. From it, modern gamblers too might learn; at the same time, they would do well to ponder the fact that much of Cardan's life was spent in wretchedness and poverty.

Among the four plates which illustrate this work is the well known 'Card Players,' which Professor Oystein Ore, in common with others, looks upon as being probably the work of Zuccaro. It is likely, however, that this is in fact one of four identical pictures—one for each of the card players portrayed—all of which may still exist, painted by John Bettes (*c.*1520–80).

T. I. WILLIAMS

NUCLEAR PHYSICS

Nuclear Physics, *by W. Heisenberg. Pp.* 224. *Methuen and Company Limited, London.* 1953. 12*s.* 6*d. net.*

This is an English translation of a series of lectures revised in 1948, intended, in the author's words, 'for readers who, while interested in natural sciences have no previous training in theoretical physics and yet are familiar to a certain extent with physical ideas.'

It does indeed start right from the beginning, dealing with atoms and molecules, as well as electrons, protons, and neutrons. Classical radioactivity is well described, and there is a good and thorough account of the relation between the mass or the binding energy of a nucleus and the numbers of protons and neutrons which it contains. Considering that no mathematics are used, a remarkably clear statement is given of the main features of the forces that hold nuclei together, and of some theories which try to explain them. On the other hand, more might perhaps have been made of energy levels. The chapter on experimental methods, though too short to give more than the barest outline, should help to make the theory more real. There is a good account of applications up to the date of the revision of the text, and a reprint of Heisenberg's article in 'Nature' in 1947 describing the German atomic energy work during the war. In most respects this book can be recommended as very well suited to the class of reader for whom it is intended, and, as might be expected from its author, it contains much to stimulate thought in those whose knowledge of the subject goes a good deal farther.

I must, however, object to some points in the historical survey. The Epicureans, as exemplified by Lucretius, did not regard the world as determinist. On the contrary, they introduced a curious kind of arbitrary deviation of the moving atoms, which Lucretius (II, 292) called *clinamen*, and which anticipated in a most remarkable way Heisenberg's own 'uncertainties,' for the precise purpose of breaking the causal sequence 'lest cause follow cause for ever.' Lucretius even went so far as to use this hypothesis to explain free will:

> *Unde est haec inquam fatis avolsa potestas*
> *per quam progredimur quo ducit quemque voluntas.*
>
> —Luc. II, 258

> 'From this I say we snatch from fate the power,
> That each may walk where his own will may lead.'

Finally, why cite Hittorf as the discoverer of the charge-mass ratio of cathode rays? Whatever preliminary work he may have done, it was not comparable with the classical experiments of J. J. Thomson or those of Weichert or of Kaufmann.

G. P. THOMSON

Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review.)

AGRICULTURE

Insecticides and Colonial Agricultural Development, *edited by T. Wallace and J. T. Martin. Proceedings of the Sixth Symposium of the Colston Research Society,* 1953. *Pp.* 169. *Butterworths Scientific Publications, London.* 1954. 30*s. net.*

Soil, *by G. V. Jacks. Pp.* 221. *Thomas Nelson and Sons Limited, London.* 1954. 12*s.* 6*d. net.*

ASTRONOMY

Nébuleuses Galactiques et Matière Interstellaire, *by J. Dufay. Pp.* 492. *Editions Albin Michel, Paris.* 1954. *Fcs* 1650 *net.*

BIOCHEMISTRY

Biochemical Preparations, Vol. 3. *Editor-in-chief E. E. Snell. Pp.* 128. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1953. 28*s. net.*

The Biochemistry of Genetics, *by J. B. S. Haldane. Pp.* 144. *George Allen and Unwin Limited, London.* 1954. 15*s. net.*

Convegno sulle Vitamine—Milano, 1953. *Pp. lix* + 883 + *xxvii. Consiglio Nazionale delle Ricerche, Rome.* 1953. *Lire* 4000.

Mécanismes Biochimiques de l'Activité des Antibiotiques, *by M.-M. Janot and J. Keufer. Pp.* 74. *Masson et Cie., Paris.* 1954. *Fcs* 670 *net.*

Principles of Biochemistry: A Biological Approach, *by M. V. Tracey. Pp.* 194. *Sir Isaac Pitman and Sons Limited, London.* 1954. 20*s. net.*

BIOLOGY

Evolution as a Process, *edited by Julian Huxley, A. C. Hardy, and E. B. Ford. Pp.* 367. *George Allen and Unwin Limited, London.* 1954. 25*s. net.*

Mammalian Hybrids, *by Annie P. Gray. Pp.* 144. *Commonwealth Agricultural Bureaux, Farnham Royal, Bucks.* 1954. 21*s. net.*

Synthetische Artbildung, *by H. Nilsson. Pp.* 1303. *C. W. K. Gleerup, Lund.* 1953. *Two volumes. Paper covers, Skr.* 225; *bound, Skr.* 250 *net.*

Viruses. *Cold Spring Harbor Symposia on Quantitative Biology, Vol. XVIII. Pp.* 301 + *xvi. The Biological Laboratory, Cold Spring Harbor, New York.* 1954. $8 *net.*

BOTANY

Bibliographie der Pflanzenschutz-Literatur, Volumes I and II, 1940–45, *by J. Bärner. Pp.* 1308. *Verlag Paul Parey, Berlin.* 1953. *D.M.* 97.

Growth and Differentiation in Plants, *edited by W. E. Loomis. Pp.* 458. *The Iowa State College Press, Iowa.* 1953. 56*s.* 6*d. net.*

New Concepts in Flowering-plant Taxonomy, *by J. Heslop-Harrison. Pp.* 135. *William Heinemann Limited, London.* 1953. 6*s. net.*

Plants for Man, *by R. W. Schery. Pp.* 564. *George Allen and Unwin Limited, London.* 1954. 70*s. net.*

CHEMISTRY

Chemical Nomenclature; Symposium on Chemical Nomenclature, September 1951. *Pp.* 112. *American Chemical Society, Washington, D.C.* 1953. $2.50 *net.*

Chemistry of the Defect Solid State, *by A. L. G. Rees. Pp.* 136. *Methuen and Company Limited, London; John Wiley and Sons Inc., New York.* 1954. 8*s.* 6*d. net.*

The Chemistry of the Morphine Alkaloids, *by K. W. Bentley. Pp.* 433. *Oxford University Press, London.* 1954. 50*s. net.*

Experimental Inorganic Chemistry, *by W. G. Palmer. Pp.* 577. *Cambridge University Press, London.* 1954. 50*s. net.*

Hydrocarbons from Petroleum, *by F. D. Rossini, B. J. Mair, and A. J. Streiff. Pp.* 556. *Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1954. 148*s. net.*

A New Periodic Table of the Elements, *by S. I. Tomkeieff. Pp.* 30. *Chapman and Hall Limited, London.* 1954. 10*s. net.*

GENERAL

Conversation with the Earth, *by H. Cloos (translated from the German by E. B. Gartside). Pp.* 427. *Routledge and Kegan Paul Limited, London.* 1954. 30*s. net.*

Elektrische Triebfahrzeuge, Vol. I and II, *by Karl Sachs. Pp. xv* + 700, *and xii* + 696 *respectively. Verlag Huber und Co. A.G., Frauenfeld.* 1953. *Swiss fcs* 65 *each volume.*

Let There Be Bread, *by Robert Brittain. Pp.* 263. *Spalding and Levy Limited, London.* 1953. 12*s.* 6*d. net.*

Petrography. An Introduction to the Study of Rocks in Thin Sections. *Pp. x* + 406. *W. H. Freeman and Company, San Francisco; Bailey Bros. and Swinfen Limited, London.* 1954. 56*s. net.*

Rocks and Mineral Deposits, *by P. Niggli (English translation by R. L. Parker). Pp. xiii* + 559. *W. H. Freeman and Company, San Francisco; Bailey Bros. and Swinfen Limited, London.* 1954. 102*s. net.*

HISTORY OF SCIENCE

Great Discoveries by Young Chemists, *by J. Kendall. Pp.* 231. *Thomas Nelson and Sons Limited, London.* 1953. 12*s.* 6*d. net.*

Nature and the Greeks, *by E. Schrödinger. Pp.* 97. *Cambridge University Press, London.* 1954. 10*s.* 6*d. net.*

PHYSICS

Acoustics, *by T. M. Yarwood. Pp.* 346. *Macmillan and Company Limited, London.* 1953. 15*s. net.*

Analysis of Deformation, Vol. I: Mathematical Theory, *by K. Swainger. Pp.* 285. *Chapman and Hall Limited, London.* 1954. 63*s. net.*

Annual Review of Nuclear Science, Vol. 3, 1953. *Pp.* 412. *Annual Reviews Inc., Stanford, California.* 1953. $7 *net.*

Discontinuous Automatic Control, *by I. Flügge-Lotz. Pp.* 168. *Princeton University Press, Princeton; Geoffrey Cumberlege, London.* 1954. 32*s.* 6*d. net.*

Elementary Introduction to Molecular Spectra, *by B. Bak. Pp.* 125. *North Holland Publishing Company, Amsterdam.* 1954. *Fl.* 9 *net.*

Nuclear Moments, *by N. F. Ramsey. Pp.* 169. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1954. 40*s. net.*

Report on the Atom, *by G. Dean. Pp.* 288. *Eyre and Spottiswoode Limited, London.* 1954. 16*s. net.*

The Revolution in Physics, *by L. de Broglie. Pp.* 310. *Routledge and Kegan Paul Limited, London.* 1954. 18*s. net.*

TECHNOLOGY

British Plastics Year Book 1954. *Pp.* 600. *Iliffe and Sons Limited, London.* 1954. 30*s. net.*

Forest Products Research and Industries in the United States, *by W. W. Varossieau. Pp. xii* + 796. *J. M. Meulenhoff, Amsterdam.* 1954. *Fl.* 45 *net.*

Oil in the Soviet Union, *by H. Hassmann (translated by Alfred M. Leeston). Pp.* 173. *Princeton University Press, Princeton; Geoffrey Cumberlege, London.* 1954. 30*s. net.*

The Structure of Textile Fibres. An Introductory Study. *Pp.* 165. *The Textile Institute, Manchester.* 1953. 12*s.* 6*d. net.*

Notes on contributors

E. N. da C. ANDRADE,
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Was born in London in 1887 and was educated at St Dunstan's College, the Universities of London, Manchester, and Heidelberg, and the Cavendish Laboratory, Cambridge. He served as an artillery officer in France in the war of 1914–18, and afterwards was for some years professor at the Artillery College (later the Royal Military College of Science). In 1928 he was appointed Quain Professor of Physics in the University of London. At University College he established a flourishing school of physics, known for fundamental work on the mechanical properties of the solid and liquid state, which he built up again after his laboratories had been completely destroyed by bombs in September 1940. In January 1950 he was appointed Director in the Royal Institution of Great Britain and Director of the Davy Faraday Research Laboratory, but in 1952 resigned, like his predecessor. He has a well known collection of early books on the exact sciences, and is an authority on Newton and his contemporaries. He maintains close connection with colleagues overseas, and is *Membre Correspondant de l'Académie des Sciences*. He is known for the clarity of his exposition of science, both in writing and by lectures.

D. A. WITTOP KONING,
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Was born in 1911, and studied pharmacy at the Municipal University of Amsterdam, where he has given lectures on the history of pharmacy since 1948. He is Curator of the Historical Medical-Pharmaceutical Museum of Amsterdam, and Treasurer of the *Union d'Histoire des Sciences*. His historical publications include books on Dutch mortars (*Nederlandse Vijzels*, Deventer, 1953), 'Art and Pharmacy' (Deventer, 1950), and Dutch weights. His book on Delft pharmacy pots (*Delftse apothekerspotten*, Deventer, 1954) is now in the press.

ADRIEN JAQUEROD,
Dr. Sc.,
Was born at Geneva in 1877, and in 1905 became Professor of Physics and Pure Mechanics in the University of Neuchâtel, where he is now Honorary Professor. He has published papers on gases (thermometry, molecular weight), deviations from Hooke's law, chronometry, and such properties of glasses as relate to isochronous oscillations. In 1920 he set up the *Laboratoire Suisse de Recherches Horlogères*, which he directed until 1950.

F. I. G. RAWLINS,
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Born in London, 1895; educated at the Universities of Edinburgh, Cambridge, and Marburg. Scientific adviser to the National Gallery since 1934: a deputy-keeper since 1948. Author of numerous papers in 'Technical Studies in the Field of the Fine Arts,' and other journals, dealing with the use of scientific methods in relation to paintings. Since 1951, vice-president and secretary-general of the International Institute for the Conservation of Museum Objects, and editor of 'Studies in Conservation.'

A. E. A. WERNER,
M.A., M.Sc., D.Phil.,
Was born in Dublin in 1911. He studied at Trinity College, Dublin, and at the University of Freiburg im Breisgau under Professor H. Staudinger. After graduating he was appointed lecturer, and later reader, in chemistry at Dublin University, where he carried out research on the chemistry of the ureides. Since 1948 he has been engaged as research chemist at the National Gallery, London.

SIR RUDOLPH PETERS,
M.C. (with bar), M.D., D.Sc., F.R.C.P., F.R.S.,
Was born in London in 1889 and has been Professor of Biochemistry in the University of Oxford since 1923, and Fellow of Trinity College, Oxford. He holds honorary degrees of the Universities of Paris, Liège, Amsterdam, and Cincinnati. He is an Hon. Fellow of Gonville and Caius College, Cambridge, and foreign member of several academies. He was educated at Wellington College, King's College (London), Cambridge University, and St. Bartholomew's Hospital (London). As Dunn lecturer in biochemistry at Cambridge he turned his attention to vitamin problems and later pursued them more intensively in Oxford. In 1930 came the first demonstration of the *in vitro* action of a vitamin, shown by the specific response of B_1 avitaminous pigeon's brain tissue to vitamin B_1 (thiamine). This led to the proof of the intimate connection of this vitamin with the metabolism of pyruvic acid, and to investigations on 'biochemical lesions.' Together with earlier work on arsenical compounds, a test system was provided which formed a basis for work in Oxford during the second world war, leading to the development of British anti-lewisite. As chairman of the Accessory Food Factors Committee, he took part in nutritional work during the war, and acted as chairman of the Vitamin C sub-committee concerned with the Vitamin C trials at Sheffield.

W. O. JAMES,
M.A., D.Phil., F.R.S.,
Was born in London in 1900 and was educated at Tottenham Grammar School and the Universities of Reading and Cambridge. Worked first on the potassium nutrition of plants on field plots at Rothamsted. Reader in botany in the University of Oxford, and since 1927 has led a school of teaching and research in plant physiology, especially concerned with nutrition and respiration. Director of the Oxford Medicinal Plants Scheme during the war and after, dealing with the production of drug plants in Britain and with the study of alkaloid metabolism in the Solanaceae. An editor of the 'New Phytologist.' Has published 'The Biology of Flowers' (with A. R. Clapham), 'Plant Respiration,' some well known text-books, and numerous papers in several branches of botany.

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